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Abstracts

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Growth factors in renal disease. *A. Fogo, Vanderbilt University Medical Center, Nashville, Tennessee, USA.* Clinical and experimental studies have demonstrated tight correlation between glomerular size and sclerosis. Many factors enhance both growth of glomerular cells (hypertrophy and hyperplasia) and extracellular matrix release. Thus, increase in glomerular size may be taken as a marker of augmented growth stimuli with the potential to increase matrix accumulation, a key step in development of glomerulosclerosis. Glomerular size was measured morphometrically in pediatric patients with apparent minimal change disease on an initial biopsy. Those patients who subsequently progressed to overt focal segmental glomerulosclerosis had significantly greater glomerular size than age-matched normal control or children who did not develop sclerosis. The relationship of these parameters was studied further in rats with ureteral diversion of one kidney and partial nephrectomy of the contralateral kidney, compared to 5/6 nephrectomy, a model of progressive glomerulosclerosis. Both groups had similar increased glomerular capillary pressure and hyperfiltration. Significant increase in glomerular size and glomerulosclerosis developed only after 5/6 nephrectomy. These observations in humans and animals pointed to the link between stimuli which increased glomerular growth and sclerosis. Glomerulosclerosis is accelerated by growth stimuli. Exogenous growth hormone given to uremic or normal rats not only increased somatic growth, but accelerated glomerular growth and sclerosis significantly. Several other experimental maneuvers of clinical interest, including dietary protein content and angiotensin-converting enzyme inhibitor (ACEI) modify glomerular growth and sclerosis in parallel. Delayed therapy with ACEI or an angiotensin II receptor antagonist (AIIRA) also ameliorated glomerulosclerosis in the non-hypertensive puromycin nephropathy (PAN) model. ACEI, in contrast to AIIRA, also decreased acute nephrotic phase proteinuria by its non-AII effects on bradykinin. Therapy limited to this acute nephrotic phase with ACEI or AIIRA did not, however, affect the subsequent glomerulosclerosis. Thus, glomerulosclerosis, but not acute proteinuria, involves endogenous angiotensin II actions. Population groups are heterogeneous not only in risk for progression of renal diseases, but also in baseline renal morphology. Thus, glomerular size in healthy African Americans was significantly larger than in Caucasians, with different distribution patterns in the two groups. Differences in genotype and/or glomerular number may underlie these findings. Of note, glomeruli are heterogeneously involved by sclerosis, with spared glomeruli demonstrated in human FSGS by serial section analysis. Further, the pattern was more focal with smaller, peripheral lesions in children than in adults, which may have implications for response to therapy. The responsiveness to ACEI in animal studies varied among the heterogeneously affected nephrons. Thus, ACEI started at 8 weeks after 5/6 nephrectomy prevented progression of early lesions, in contrast to continued progression of more advanced lesions. Higher doses of ACEI were more beneficial, even reversing sclerosis. Inhibition of AII may also impact other growth factors. Different growth factors appear to be pivotal at different stages of injury. Expression of platelet-derived growth factor B-chain (PDGF-B) was increased in early glomerulosclerosis, but was not uniformly distributed among the heterogeneously affected glomeruli. Immunostaining showed that increased protein was restricted to those glomeruli with early sclerosis. Treatment with angiotensin II receptor antagonist decreased both PDGF-B chain expression and glomerulosclerosis, whereas non-specific antihypertensive treatment did not normalize either parameter. Further study of the complex interactions of these and other growth factors will form the scientific rationale for effective therapeutic interventions.

Water channels in the kidney. *S. Nielsen, M. Knepper, and P. Agre, University of Aarhus, Denmark; National Institutes of Health, Bethesda, Maryland, USA; Johns Hopkins University, Baltimore, Maryland, USA.* The longstanding biophysical question of how water crosses plasma membranes, and how this transport is regulated, was answered by the recent discovery of Aquaporin water channels. Aquaporin 1 is the archetypal member of this large family of membrane water transporters known as the "Aquaporins" (AQPs). AQP1 is abundant in the apical and basolateral membranes of renal proximal tubules and descending thin limbs in kidney, and represents the major constitutive water channel of the nephron, where most of the 170 liters of water are reabsorbed per day. AQP1 is also present in a number of extra renal epithelia. In the renal collecting duct, the site for vasopressin regulation of body water balance, AQP2 is localized in the apical plasma membrane and in intracellular vesicles. Vasopressin increases the water permeability by vasopressin-induced targeting of AQP2 in vesicles to the apical plasma membranes. Furthermore, AQP2 is regulated by long-term mechanisms. Dehydration and increased levels of vasopressin cause a marked increase in AQP2 expression, resulting in higher water reabsorptive capacity. Correspondingly, acquired forms of diabetes insipidus (for example, induced by lithium treatment) is associated with markedly reduced levels of AQP2. Thus, AQP2 is the predominant vasopressin sensitive water channel, and AQP2 is essential for regulation of body water balance. AQP3 and AQP4 are abundant in the basolateral plasma membranes of the collecting principal cells, representing the exit pathway for water. Furthermore, AQP4 has been shown to be abundant in brain in hypothalamic nuclei, indicating a role for osmosensing, whereas AQP5 has been shown to be expressed in salivary glands and lung indicating a role for water transport at these sites. AQPs exist as tetramers which are comprised of functionally independent subunits. Continued analysis of the Aquaporins is providing detailed molecular insight into the fundamental physiological problems of water balance and water balance disorders.

Factor H deficiency in pigs causes lethal membranoproliferative glomerulonephritis (MPGN) type II. *K. Høgåsen, J.H. Jansen, T.E. Mollnes, A.M. Grøndahl, and M. Harboe, Institute of Immunology and Rheumatology, University of Oslo, Norwegian College of Veterinary Medicine, Oslo, Nordland Central Hospital Bodø, and University of Tromsø, Tromsø, Norway.* We have recently described hereditary MPGN type II in pigs. Affected animals had persistent hypocomplementemia (C3 ~ 10% of normal) and massive glomerular complement deposits. They all ($N = 25$) developed nephritis and eventually died of renal failure within 72 days of birth (median 37). In the present study we investigated the cause of the disease. Transfusion of normal porcine plasma to 13 affected piglets inhibited complement activation and increased median survival to 82 days (max. 375). The active component of normal plasma was isolated and demonstrated to be factor H, a complement regulatory protein. An extended breeding study showed autosomal recessive inheritance. Heterozygous animals had half-normal plasma level of factor H, determined by a novel enzyme immunosassay, whereas deficient animals had only about 2% compared with their homozygous healthy littermates. There was an absolute concordance between factor H deficiency and MPGN type II; all of 64 factor H deficient piglets developed MPGN type II, in contrast to none of their 175 factor H

sufficient littermates. Until now 14 cases of *human* factor H deficiency have been described. Several of these had MPGN type II. Furthermore, most cases of human MPGN type II are associated with C3 nephritic factor, an autoantibody blocking factor H function. Thus, it is concluded that deficient factor H activity causes MPGN type II in human beings as well as in pigs.

Glomerulopathy associated with predominant fibronectin (FN) deposits. A newly recognized hereditary disease. *E.H. Strøm, R. Krapf, F. Gloor, J. Neuweiler, G. Banfi, G. Mazzucco, G. Monga, A.B. Abt, L.A. Hebert, D.D. Sedmak, R. Riess, P. Stosiek, F. Gudat, and M.J. Mihatsch, Institute for Pathology, University of Basel, Department of Medicine and Institute of Pathology, Cantonal Hospital, St. Gallen, Switzerland, Department of Nephrology, Maggiore Hospital, Milan, Department of Biomedical Science and Human Oncology, University of Torino, Italy, Department of Pathology, M.S. Hershey Medical Center, Pennsylvania State University, Hershey, Department of Medicine and Department of Pathology, Ohio State University, Columbus, Ohio, USA, Institute of Pathology, Klinikum Nürnberg, Institute of Pathology, Carl-Thiem Klinikum, Cottbus, Germany, Department of Pathology, Ullevål University Hospital, Oslo, Norway.* A newly recognized type of familial glomerulopathy, observed in patients of both sexes in six families, is reported. Proteinuria, often within the nephrotic range, microscopic hematuria, hypertension, and a slowly decreasing renal function over several years, were common. No underlying systemic diseases were identified. LM showed enlarged glomeruli with minimal hypercellularity with extensive deposits in the mesangium and subendothelial space. By EM, granular deposits with some admixture of fibrils were most common. In one family, the deposits were predominantly fibrillary. Immunoglobulins and complement factors were inconstant or lacking. A main finding was a strong immune reactivity to FN, corresponding to the distribution of the deposits. In one patient, the deposits recurred in a renal transplant. There was no indication of systemic deposition. Abnormalities in the metabolism of circulating FN may play a pathogenetic role in this disease of probable autosomal dominant inheritance.

Influence of interleukins on human renal tubular cells in culture. *J. Ladefoged and H. Blaehr, Department of Nephrology, Rigshospitalet, Copenhagen, Denmark.* The renal allograft rejection is characterized by invasion of the tissue with mononuclear cells and production of huge amounts of interleukins in the tissue. The effect of interleukins on the immunologically active cells is well-known, whereas their interactions with the renal tubular cells are uncertain. Tubular cell lines were therefore established from renal biopsies in patients with renal disorders, mainly chronic glomerulonephritis and renal transplants. The cells formed a monolayer with characteristics of renal epithelium. The culture medium was RPMI with fetal calf serum, pyruvate, insulin, EGF, transferrin, and glucose. The proliferation rate of the renal cells was measured by C^{14}thymidine uptake at fixed times after subcultivation of the cells in a medium with RPMI and 10% fetal calf serum or 2% Ultroser ^{R}G (serum-free medium). Interleukin(IL)-1 and IL-4 in low concentrations had a marked suppressive effect on proliferation rates, but a slight proliferation of the cells was found even at very high concentrations. Low concentrations of IL-2 had a very small stimulatory effect, probably on a few passenger lymphocytes. IL-3, IL-5, IL-6, IL-7, IL-8 and IL-9 had very little effect in physiological concentrations. Epidermal growth factor, insulin-like growth factor, and insulin stimulated growth rates. Tumor necrosis factor in high concentration was suppressive. Gamma-interferon, granulocyte-colony stimulating factor, and endotoxin were inactive. Supernatant from mitogen-stimulated lymphocyte cultures, macrophage or T-cell enriched cultures from peripheral blood had a suppressive effect, due probably to the content of interleukins.

Cardiovascular complications and renal disease. *C. Grönhagen-Riska, J. Fagerudd, P.H. Groop, K. Metsärinne, S. Stenman, and K. Tötterman, Division of Nephrology, Department of Medicine, Helsinki University Hospital, Helsinki, Finland.* Morbidity and mortality of patients with long standing renal failure are dominated by cardiovascular complications. Numerous sources indicate 40–50% mortality of cardiovascular causes among patients with end-stage renal disease. There are numerous reasons for this outcome, such as hypertension, lipid changes, anemia, electrolyte disturbances, secondary hyperparathyroidism, unfavorable hemodynamic changes during hemodialysis, and weight gain between dialysis sessions. Other possible pathogenetic factors, such as β_2-microglobulin, advanced glycosylation products (particularly in diabetics), insulin resistance, "uremic toxins," dialysis efficacy, and bioincompatibility remain unresolved and need to be studied further. Individual impact of the different risk factors remains unclear, and there are very few long-term, prospective, randomized intervention studies. Data from the Finnish Registry for Kidney Diseases from 1,993 included 109 myocardial infarctions and 60 strokes among 2,211 patients either on dialysis therapy or living with a functioning graft. Significant associations between these complications were diabetes, other cardiovascular diseases, low serum albumin, high phosphorus, and low hematocrit. No associations were found between myocardial infarction, antihypertensive therapy or high blood pressure, but there was hypertension associated with stroke. In a prospective study, which started in 1987–88, we have followed 57 consecutive predialysis patients (17 had diabetes). Initial cardiovascular examinations included an M-mode echocardiogram and a dynamic exercise test. Twenty-five of the patients have died, and 11 of these had diabetes. Variables significantly associated with mortality were higher age, higher NYHA classification, higher systolic blood pressure, higher atrial natriuretic peptide (ANP) levels, and shorter exercise time. However, echocardiogram findings did not differ significantly between those who died and survivors. Hemoglobin and K were higher in the survivors, who also had higher creatinine, urea and albumin values, although creatinine clearance values were similar. These findings may indicate better initial nutritional status of survivors. Ten of 17 deaths were attributed to cardiovascular causes, and these patients initially had significantly lower exercise time. Diabetes is a significant risk factor and initial studies indicated that those diabetics who would die within the FU period had progressed faster in the predialysis phase, and risk factors observed in these were similar to those found in the whole patient population. However, diabetics with a poor prognosis had a higher left atrial diameter and lower ejection fraction than surviving diabetics. Although not all these patients died from cardiovascular complications, an originally compromised cardiac status predicted a high mortality risk. Intervention should be directed at diabetes patients at a very early stage of their disease. We have studied hereditary associations between different groups of IDDM patients and results indicate that patients who develop diabetic nephropathy (and later cardiovascular complications) come from families with higher diastolic blood pressure and greater insulin resistance when compared with families of patients with uncomplicated diabetes. These results open new possibilities to identify diabetics at risk and to study the pathogenesis of cardiovascular complications.

Moderate α_1-antitrypsin deficiency—A prognostic factor in PR3-ANCA vasculitis. *M. Segelmark, A-N. Elzouki, J. Wieslander, and S. Eriksson, Department of Nephrology, Lund, Department of Medicine, Malmö, Lund University, Wieslab AB, Lund, Sweden.* **Aim:** To ascertain the clinical importance of moderate α_1-antitrypsin (α_1-AT) deficiency among patients with PR3-ANCA-positive vasculitis. **Methods:** α_1-AT phenotyping was performed on 105 PR3-ANCA-positive sera. Clinical data were collected retrospectively for 100 of these patients. **Results:** Eighteen patients (17%) were positive for the PiZ variant of α_1-AT (one homozygote and 17 heterozygotes), as compared to 4.7% for the general Swedish population ($P < 0.001$). Vasculitic disease was diagnosed in 99 cases. At presentation the median α_1-AT concentration was lower in the PiZ-positive group, 1.6 g/liter as compared to 3.2 g/liter ($P < 0.01$), but there were no significant differences in other parameters of inflammation, such as ESR, CRP, albumin, hemoglobin, or white blood cell count. Overall 94% of the patients had signs of renal involvement; there were no significant differences in the median S-creatinine concentration ($P = 0.23$). Median score for organ involvement was 5.5 for the PiZ-positive compared to 4 for the PiZ-negative group ($P < 0.01$). No difference was detected in tendency to relapse; approximately half of the patients who achieved remission had experienced a relapse after four years of follow-up. Twenty deaths were recorded (7/18 in the PiZ-positive and 13/81 in the PiZ-negative group; $P = 0.048$). The difference in survival was significant also when the analysis was restricted to the 66 patients included in the study at onset of disease and using the log-rank test ($P = 0.016$). **Conclusion:** Patients with PR3-ANCA-positive vasculitis who carry the PiZ allele for α_1-AT have a more disseminated disease and a worse prognosis. This indicates a protective role for α_1-AT in this disease and gives indirect support for the notion that proteolytic enzymes such as PR3 (which are normally inhibited by α_1-AT) have a role in the pathogenesis of vasculitis.

Increased urinary transforming growth factor β1 (TGF-β1) in glomerular diseases. *E. Honkanen, A-M. Teppo, and C. Grönhagen-Riska, Helsinki University Central Hospital, Department of Medicine, Division of Nephrology, Helsinki, Finland.* Production of extracellular matrix, wound repair, and tissue remodeling are regulated by TGF-β, a cytokine produced by most nucleated cells and thrombocytes. It has also been suggested to have an essential role in the development of glomerular sclerosis. We measured urinary TGF-β1 by double antibody EIA in 33 patients with idiopathic membranous glomerulonephritis (MGN), 10 with IgA nephropathy (IgAN), 6 with systemic vasculitis (VAS), 17 with diabetic nephropathy (DNP), and 17 normal controls (NC). Compared with the NC (37 ± 11 pg/mg creatinine, mean ± SE), highly increased urinary TGF-β1 was found both in patients with MGN (248 ± 57, $P < 0.001$), IgAN (151 ± 51, $P = 0.01$), VAS (294 ± 79, $P < 0.001$) and with DNP (612 ± 124, $P < 0.001$ vs. NC; <0.04 vs. MGN). Urinary TGF-β1 levels did not correlate with protein excretion, serum creatinine or albumin concentration. In MGN TGF-β1 excretion >300 pg/mg creatinine was often associated with a progressive disease (decreasing GFR) while all patients with an excretion of <300 pg/mg creatinine had a stable clinical course ($P < 0.001$). Immunosuppressive treatment in 5 MGN patients decreased TGF-β1 excretion from 835 ± 347 to 93 ± 24 pg/mg creatinine ($P = 0.071$). The results suggest that urinary TGF-β1 excretion is increased in inflammatory and noninflammatory glomerular diseases. It may serve as an indicator of ongoing sclerosing processes in the kidneys.

Anti-SS-A antibody associated urolithiasis and distal renal tubular acidosis, preceding primary Sjögren's syndrome. *P. Eriksson and T. Denneberg, Department of Internal Medicine, Hospital of Jönköping and Department of Urology, University Hospital, Linköping, Sweden.* Distal renal tubular acidosis (dRTA) is a risk factor for calcium stone formation and can be associated with autoimmune diseases such as primary Sjögren's syndrome (SS). SS is characterized by keratoconjunctivitis sicca and xerostomia, and autoantibodies such as anti-SS-A and anti-SS-B are common. The aim of this study was to investigate clinical and laboratory evidence of SS in patients with urolithiasis and dRTA. **Material and methods:** We studied ten female patients, who presented with urolithiasis and dRTA but without sicca symptoms (urolithiasis group). Sixteen SS patients (15 females, 1 male) without urolithiasis or known dRTA, who first presented with sicca symptoms, served as a reference group. The criteria described by Daniels and Talal were used for the diagnosis of SS and possible SS. Renal acidification capacity was evaluated with ammonium chloride loading. Kidney biopsies were performed in five patients in the urolithiasis group and in four patients in the reference group. **Results:** Definite or possible SS developed in 7 of the 10 patients, 1–48 years after the onset of urolithiasis. Anti-SS-A was present in 8/10 and anti-SS-B in 5/10 in the urolithiasis group. Occurrence of SS-related symptoms and autoantibodies did not differ between the groups. Varying degrees of tubulointerstitial nephritis were found in 4/5 in the urolithiasis group and in 2/4 (with dRTA) in the reference group. **Conclusions:** Urolithiasis and dRTA can precede SS, and patients with dRTA may have SS in the absence of subjective sicca symptoms. Anti-SS-A antibodies are common in female patients with urolithiasis and dRTA. Therefore, we propose using the term "Sjögren-related renal disease" in these patients.

Autoantibodies and primary Sjögren's syndrome in a hypocitraturic stone population. *P. Eriksson and T. Denneberg, Department of Internal Medicine, Hospital of Jönköping, and Department of Urology, University Hospital, Linköping, Sweden.* Primary Sjögren's syndrome (SS) can be complicated by renal involvement and distal renal tubular acidosis (dRTA), which is mostly associated with hypocitraturia. Both are risk factors for calcium stone formation. Increased levels of serum IgG and autoantibodies (anti-SS-A and ANA) are common in patients with SS, as well as in patients with dRTA, and dRTA can be associated with immune-mediated diseases. The aim was to look for autoantibodies and autoimmune diseases, especially SS, in a large hypocitraturic stone population. **Material and Methods:** From a population of 1500 stone formers 197 patients with hypocitraturia (67 females and 130 males, mean age 56 and 55 years, respectively) were studied with respect to ANA and serum IgG. Anti-SS-A antibodies were investigated in a subgroup of 46 females. SS was diagnosed according to the criteria proposed by Daniels and Talal. **Results.** ANA was present in 1.5% of the males and in 17.9% of the females. Isolated high levels of serum IgG were present in 9.0% of the males and in 3.0% of the females. Anti-SS-A antibodies were estimated to be present in about 17% of all females. Four of 14 females examined fulfilled the criteria of SS or possible SS, whereas no male had SS. Other autoimmune diseases, such as chronic autoimmune hepatitis, thyroid diseases and rheumatoid arthritis, were also present. **Conclusion.** In hypocitraturic female stone formers, autoantibodies such as anti-SS-A and ANA were rather common. Some of these patients also had SS or other autoimmune diseases. We recommend that anti-SS-A antibodies should be analyzed in female hypocitraturic stone formers.

Focal segmental glomerulosclerosis—Familial and sporadic forms. *M. Felldin, G. Nordén, C. Svalander, and G. Nyberg, Department of Nephrology, Sahlgrenska University Hopsital, Göteborg, Sweden.* The impact of the underlying renal disease on outcome of renal transplantation (Tx) was retrospectively investigated in 1,000 consecutive transplant patients in Göteborg (1985–1993). This study presents the 16 patients with biopsy-verified focal segmental glomerulosclerosis (FSGS) who received 23 transplants. Eight of 16 FSGS patients had a family history of FSGS and the father of one additional patient died with uremia. Seven cases were sporadic. The hereditary cases were members of 7 separate families. Patients were followed for 2–9 years after Tx, median: 5.

	Hereditary	Sporadic
Gender, M/F	8/1	4/3
Age at onset of symptoms (mean ± SD)	14 ± 8	29 ± 17[a]
Age at ESRF	34 ± 9	36 ± 16
Immunotherapy before Tx	1	5[a]
Number of grafts	12	11
Kidney source, cadaveric/living	6/6	8/3
Number of grafts lost (of rejection)	6 (4)	6 (2)
Number of grafts with recurrence	0	5[b]

[a] $P = 0.03–0.05$
[b] $P = 0.01$

Conclusion: The hereditary form of FSGS is as frequent as the sporadic form. The histopathology in native kidneys remains indistinguishable but the clinical picture is different. Family cases were younger at onset of proteinuria, but their rate of progression was slower and no patient had recurrence of FSGS after Tx. Consequently, the risk of recurrence for patients with sporadic FSGS is higher than previously thought.

Fifteen years of renal replacement therapy. *T. Leivestad, for The Norwegian Renal Registry, The National Hospital, Oslo, Norway.* Since 1980, follow-up data for all Norwegian patients starting renal replacement therapy (RRT) for chronic renal failure have been entered into a national registry. The yearly acceptance rate has increased steadily, from 40 to 72 (mean 52.6) per million inhabitants. This is mainly due to acceptance of older patients: in 1980 5% of new patients were over 70 years; in 1994 they constituted 30%. A majority (64%) were males. The dominant cause of renal failure was glomerulonephritis (34%); diabetic nephropathy accounted for 12.5%, with no increase over the period. At the start of RRT, 82% were considered to be potential candidates for transplantation. Initial treatment was hemodialysis in 77%, peritoneal dialysis in 8%, and predialytic transplantation in 15%. The 18 Norwegian renal units had quite different acceptance rates: the mean number of new patients per million/year was 39 in the lowest and 82 in the center with the highest rate. For diabetics the corresponding figures varied between 2.8 and 11.7 per million/year. Patient survival (Kaplan-Meier) was 75.2% at one year, 49.7% at five years, and 35% at ten years. Among the 1,755 reported deaths, in 41% this was due to cardiac causes, cerebrovascular disease in 12%, infections in 18% and malignant disease in 8%.

Will low grade proteinuria increase to high grade proteinuria in patients with IgA nephropathy? *R. Sakari, Department of Renal Medicine, Huddinge University Hospital, Karolinska Institute, Stockholm, Sweden.* A high degree of proteinuria (PU) is perhaps the best prognostic indicator of progressive renal disease in IgA nephropathy (IgAN). In a previous report we found that 15 of 75 patients with high PU (>1 g/24 hr) developed end-stage renal disease (ESRD). Ten years after renal biopsy (RB) the actuarial renal survival was 61%. Of the patients with high PU >80% became hypertensive during the study. In the present study our aim was to detect a possible increase in PU during follow-up in patients with low

grade PU at time of RB as an indicator of progressive disease. **Results:** At time of RB, 111 patients had PU >1 g/24 hr. Thirty-two of these have progressed to ESRD. In 116 patients the PU was <1 g/24 hr (0.27 ± 0.48). Ten of these have increased the PU to high PU. Mean follow-up was 4 years (range 1–10) to develop high PU in these ten patients. All but one of the ten became hypertensive during follow-up. One hundred six patients with low PU remained so. Their initial PU was 0.19 ± 0.28 g/24 hr and mean age 29.2 years at time of renal biopsy. They had a slight increase in PU to 0.24 ± 0.35 (NS) with a follow-up of 10 years. Of the patients 11 had PU >0.8 g/24 hr and seemed to have a progressive disease. Twenty-nine of the patients with low PU became hypertensive. **Conclusions:** In most patients IgAN is a slowly progressive disease. A high degree of PU and hypertension are well-known indicators of a poor prognosis. Many of the patients with initial high PU developed hypertension and ESRD. They were older at the time of renal biopsy and perhaps found later in their disease than patients with low PU. It seems that there is a slow increase of proteinuria in patients with initially low PU since 10 of 116 have developed high PU and several others have slowly increasing PU. The fact that 29 patients with low PU were regarded hypertensive may reflect a more aggressive antihypertensive treatment than earlier. This may also explain the slowly increasing PU, since ACE inhibitors have been the drug of choice in our patients with nephritic diseases. It seems that only studies over 3 or 4 decades or more will reveal the real prognosis in IgAN. In all older patients entering ESRD today IgAN is a possible cause of ESRD.

Improvement in renal function by a calcium entry blocker (felodipine) in cyclosporine treated patients in acute and short-term studies. *E.B. Pedersen, J.K. Madsen, S.S. Sørensen, and H. Zachariae, Department of Medicine and Nephrology C, Skejby Hospital and Department of Dermatology, Marselisborg Hospital, University Hospitals in Aarhus, Denmark.* The purpose was to study whether the calcium entry blocker, felodipine, could reduce the nephrotoxic and hypertensive effect of cyclosporine. The effect of felodipine on glomerular filtration rate (GFR), renal plasma flow (RPF), fractional excretion of sodium, lithium clearance and blood pressure was measured in three randomized, placebo-controlled studies of cyclosporine treated patients. In study one 10 renal transplant recipients were examined within the first six months after transplantation in a cross-over design with determination of renal hemodynamics after acute injection of felodipine or placebo, with an interval less than one week between the two examinations. In study two 79 renal transplant recipients were randomized to treatment with felodipine or placebo just before transplantation, and renal hemodynamics were determined after twelve weeks. In study three 18 patients, treated with cyclosporine due to dermatological diseases, were examined in a cross-over design with determination of renal hemodynamics after four weeks of treatment with felodipine or placebo. Felodipine increased renal hemodynamics in study one (GFR: 16%, RPF: 33%, $P < 0.01$ for both), in study two (GFR: 23%, RPF: 28%, $P < 0.05$ for both), and in study three (GFR: 13%, RPF: 26%, $P < 0.01$ for both). FE-Na was significantly increased by felodipine in study one and three, but not in study two. Lithium clearance was significantly increased and blood pressure significantly reduced by felodipine in all three studies. It can be concluded that felodipine counteracts both the cyclosporine induced impairment in renal hemodynamics and the increase in blood pressure in acute and short-term studies.

OKT3 in steroid resistant rejections in renal transplant recipients. 2.5 mg vs. 5.0 mg. *K. Midtvedt, A.B. Tafjord, K.P. Nordal, B. Draganov, T.C. Eide, A. Hartmann, K.J. Berg, H. Holdaas, and P. Fauchald, Medical Department B, National Hospital, Oslo, Norway.* **Aim:** To compare the effect of 2.5 mg vs. 5 mg OKT3 as therapy in renal transplant recipients with steroid resistant rejections. **Methods:** Thirty renal transplant recipients, with renal biopsy verified rejections not responding to i.v. methylprednisolone, were randomized to receive either 2.5 mg or 5.0 mg OKT3 i.v. for 10 days (15 in each group). **Results:** Three grafts were lost due to rejection within the first 3 months following OKT3, one in the 2.5 mg group and two in the 5 mg group. In addition two grafts were lost in the 2.5 mg group (cerebral infarction and death with functioning graft/coronary infarction and coronary surgery).

	T cell response (CD2 pos)		
	Day 0	Day 1	Day 6–10
2.5 mg	140	14[a]	41
5.0 mg	140	38	34

[a] $P < 0.001$ vs. 5.0 mg, after start of OKT3

	Serum creatinine, *μmol/liter* (±SD)				
	Stable creatinine before rejection	At start of OKT3	Maximum creatinine	At stop of OKT3	After 3 months
2.5 mg	187 (51)	296 (84)	326 (105)	199 (57)	203 (71)
5.0 mg	197 (43)	302 (51)	362 (75)	205 (49)	198 (71)

Conclusion: Within the first three months two grafts were lost in the 5.0 mg group and one graft in the 2.5 mg group due to rejection. 2.5 mg OKT3 used as rescue treatment of steroid resistant rejections is as efficient as standard 5.0 mg in renal transplant recipients.

Renal and hormonal effects of acute FK506 infusion in pigs. *C.B. Nielsen, K. Golbækdal, and E.B. Pedersen, Department of Medicine and Nephrology C, Skejby Hospital, University Hospital of Aarhus, Aarhus, Denmark.* FK506 has been shown to be an effective immunosuppressive drug with possible nephrotoxic side effects. In this study we have investigated the acute effects of FK506 on renal hemodynamics, water, sodium and lithium excretion rates and plasma levels of angiotensin II (Ang II), aldosterone (Aldo), atrial natriuretic peptide (ANP) and vasopressin (VP) in 29 Danish landrace female pigs that have a renal structure/function resembling the human kidney. A continuous intravenous infusion was given over a 2 hour period to 4 dose groups: A: 0.075 mg/kg ($N = 7$); B: 0.15 mg/kg ($N = 8$); C: 0.3 mg/kg ($N = 6$); and P: placebo vehicle ($N = 8$). Glomerular filtration rate (GFR) and renal plasma flow (RPF) were measured by constant infusion clearance technique using 125-I-iothalamate and 131-I-hippuran, and hormonal parameters were measured by radioimmunoassays. In all three FK506 groups, fractional lithium excretion was significantly decreased 2 hours after FK506 infusion (P: + 0.4%; A: − 8.8% ($P < 0.05$); B: − 12.9%; and C: − 11.2%; $P < 0.01$ for both). Mean blood pressure (MBP) was significantly increased in the two highest dosage groups (B, C) at 2 hours of infusion: (MBP; P: + 2.9%, A: + 3.5%, B: + 12.0%, C: + 15.3% ($P < 0.01$ in group B and C). GFR and RPF showed minor and inconsistent changes while all other parameters measured showed similar or no changes. It is concluded that FK506 infusion can acutely increase the mean blood pressure and decrease fractional lithium excretion in a dose-dependent manner. It is suggested that FK506 might influence the proximal tubular function.

Renal autoregulation. *K. Aukland and A.H. Øien, University of Bergen, Bergen, Norway.* Autoregulation in the kidney may be defined as the ability of the organ to maintain constant blood flow (RBF) in spite of varying arterial pressure (AP), without the assistance of vasomotor nerves or circulating vasoactive substances. It implies dilation and reduced resistance at reduced AP, localized mainly in preglomerular vessels. In several other organs such vasodilation is induced through an initial fall in blood flow, reduced tissue pO_2, or increased pCO_2. In the kidney there is no evidence for such metabolic autoregulation, simply because of great renal overperfusion relative to metabolic needs. Instead, the kidney has a unique negative feedback system which reacts to reduction of RBF and glomerular filtration rate (GFR), i.e. the tubuloglomerular feedback mechanism (TGF): when the amount of filtered sodium chloride falls, its concentration in the distal tubule and reabsorption at the macula densa is reduced. This initiates a signal to the adjacent afferent arteriole to dilate, and RBF is restored. The nature of the signal is still unclear, but it does not involve the renin-angiotensin system. While TGF may seem to be an appropriate mechanism to regulate renal salt excretion, mathematical models indicate that TGF can explain only a small part of the autoregulation of RBF and GFR. Experimental support for that conclusion comes from good autoregulation in non-filtering kidneys and after blocking TGF. The alternative is a myogenic autoregulation, i.e. contraction of vascular smooth muscle in response to increased transmural pressure. The problem is that this mechanism does not represent a negative feedback, i.e. it does

not respond to altered RBF or GFR *per se*. Mathematical models show, however, that maintenance of vascular wall tension (pressure × vessel radius) as a "set point" will create excellent autoregulation. Fairly direct evidence for a myogenic mechanism that greatly overpowers an oppositely directed TGF has been obtained by exposing the kidney to subatmospheric pressure. While the full implication of autoregulation in health and disease is not obvious, it may: (1) help to regulate salt excretion; (2) prevent detrimentally high glomerular capillary pressure; and (3) contribute to maintaining GFR at increased ureteral pressure.

Down-regulation of AQP-2 water channel expression in postobstructive polyuria. *J. Frøkiær, D. Marples, and S. Nielsen, University of Aarhus, Aarhus, Denmark.* **Aim:** Release of bilateral ureteral obstruction (BUO) is followed by increased diuresis, which may be caused by defects in both proximal and distal sodium and water transport. Recently, the Aquaporins, a novel family of membrane water channels, were identified. The effect of BUO and release of BUO on expression of the vasopressin sensitive water channel Aquoporin-2 (AQP-2) was examined in rats. **Methods:** Münich-Wistar rats (250 g) were kept in metabolic cages during the entire experiment. BUO was created by placing a 6–7 mm piece of bisected polyethylene tubing (PE-50) around each mid-ureter and tightened with a 5–0 silk ligature. Following 24 hours BUO was released by removing the ligature and the plastic tubing. Rats were allocated into groups with 24 hour BUO and release of BUO followed for 24, 48 hours and 7 days, respectively. Kidneys were then removed and membranes were prepared from the inner medulla of both kidneys. AQP-2 expression was determined by immunoblotting and densitometry. **Results:** AQP-2 expression was significantly reduced during 24 hours of BUO to 26 ± 8%. Twenty-four and 48 hours after release of BUO the reduction in AQP-2 expression persisted concurrent with the onset of a marked postobstructive polyuria (31 ± 1 to 87 ± 13 μl/min/kg). Urine osmolality was reduced from 1557 ± 182 to 392 ± 41 mOsm/kg, whereas sodium excretion increased (3.1 ± 0.4 vs. 2.0 ± 0.3 μmol/min/kg). During a recovery period of 7 days renal water and electrolyte excretion normalized, but the down-regulation of AQP-2 was only partly reversed (49 ± 14%). **Conclusion:** BUO was associated with marked reductions in the vasopressin sensitive water channel, AQP-2, coincidental with development of polyuria. This may represent an important factor in the development of postobstructive diuresis.

Mesangiolysis interferes with autoregulation of zonal GFR in SHR. *X. Wang, K. Aukland, and B.M. Iversen, Renal Research Group, Medical Department A, Haukeland Hospital and Department of Physiology, University of Bergen, Bergen, Norway.* The physiological role of mesangial cells in the regulation of glomerular hemodynamics is not fully understood. Autoregulation of renal blood flow (RBF) is normal after mesangiolysis induced by anti-thymocyte antibodies (anti-Thy1.1) in normotensive rats. This study was designed to investigate whether the contractile mesangial cells are involved in autoregulation of glomerular filtration rate (GFR), and whether the response is different in the various cortical layers in normotensive and hypertensive rats. Spontaneously hypertensive rate (SHR) and Wistar Kyoto (WKY) rats were examined 24 hours after infusion of anti-Thy1.1 antiserum, with normal mice serum being infused in controls. GFR was measured by infusion of ^{125}I aprotinin (^{125}IAp) at control arterial pressure and infusion of ^{131}IAp at the lower pressure limit of RBF autoregulation. Local GFR was estimated from aprotinin uptake in tissue samples dissected from outer, middle and inner cortex (OC, MC, IC). Mesangiolysis did not affect RBF autoregulation in either WKY or SHR. The percent reduction of total GFR during pressure reduction in WKY and SHR with mesangiolysis was 8.8 ± 1.0% vs. 8.6 ± 3.0% (P = NS), and 18.0 ± 3.3% compared with 12.3 ± 3.7% ($P < 0.05$) in control groups, respectively. After mesangiolysis, pressure reduction caused significantly greater reduction ($P < 0.05$) of zonal GFR in SHR (24 ± 2.0%, 23 ± 2.7%, 21 ± 2.2%) than in WKY (15 ± 1.5%, 12 ± 0.9%, 13 ± 2.7%). **Conclusion:** The increased number of mesangial cells in hypertensive rats may play a role in maintenance of GFR autoregulation either by an effect on K_f or by adjustment of pre- or postglomerular vascular resistance.

Atrial natriuretic factor does not inhibit pressure dependent renin release in the dog. *J.F. Bugge, P.A. Næss, and G. Christensen, Institute for Experimental Medical Research, Ullevaal Hospital and Department of Anaesthesia, Rikshospitalet, Oslo, Norway.* Two of the most important stimuli for renin release are increased renal sympathetic nerve activity and reduced renal arterial pressure (RAP). The pressure dependent renin release is mediated by a hemodynamic (autoregulatory) and a tubular (macula densa) mechanism. Renin release is stimulated by autoregulatory vasodilation and decreased NaCl delivery to, and hence reabsorption at, macula densa. Atrial natriuretic factor (ANF) inhibits renin release induced by renal nerve stimulation, and the present study was undertaken to investigate the influence of ANF on renin release induced by renal hypotension. Renin release was induced in seven barbiturate-anesthetized dogs with denervated kidneys by renal arterial constriction to an RAP of 50 mm Hg before and during intrarenal infusion of ANF (200 ng min^{-1} kg^{-1} body wt). Before ANF infusion renal arterial constriction increased renin release from 0.2 ± 0.1 to 21.8 ± 3.3 μg angiotensin I (AI) min^{-1}. During ANF infusion renal arterial constriction raised renin release to the same levels (from 0.8 ± 0.6 to 23.7 ± 4.6 μg AI min^{-1}). At control blood pressure ANF increased glomerular filtration rate from 33.9 ± 4.2 to 43.4 ± 5.6 ml min^{-1} and sodium excretion from 72 ± 22 to 567 ± 112 μmol min^{-1}. ANF was without effect on glomerular filtration and sodium excretion at low RAP. We conclude that ANF is not an inhibitor of pressure dependent renin release, either by the autoregulatory or the macula densa mechanism.

Regulation of human renal function by NO: Acute effects of L-NMMA on renal function, renal plasma flow and sodium excretion. *J.N. Bech, C.B. Nielsen, and E.B. Pedersen, Department of Medicine and Nephrology C, Skejby Hospital, University Hospital, Aarhus, Denmark.* **Background:** Numerous animal studies have implicated an important role of NO in the regulation of renal hemodynamics and sodium excretory capacity. N^G-monomethyl-L-arginine (L-NMMA) specifically blocks NO synthesis by interfering with NO synthase. The renal effects of acute NO blocade have not been investigated in humans. For the first time we describe the effects of NO blocade by L-NMMA on renal plasma flow (RPF), glomerular filtration rate (GFR), sodium excretion (U-Na), fractional sodium excretion (FE_{Na}), blood pressure (BP), and heart rate (HR) in humans. **Methods and design:** Randomized, placebo-controlled infusion study. Eighteen healthy individuals were randomized to bolus injections over 10 minutes of either L-NMMA 3 mg/kg ($N = 9$) or saline. GFR and RPF were measured using renal clearance of ^{51}Cr-EDTA and ^{125}I-hippuran. The study was divided into 7 clearance periods of 30 minutes: 3 periods during basal conditions and 4 periods after bolus injection. Experiments were performed in a fasting and supine state and subjects were exposed to a waterload of 200 ml each 30 minutes during the experiment. **Results:** GFR, RPF, U-Na, FE_{Na}, BP, and HR were not affected by placebo, but L-NMMA significantly induced a reduction of RPF at 30 minutes (503 ± 63 ml/min vs. 415 ± 79 ml/min, $P < 0.01$) persisting for 2 hours, a reduction of U-Na (315 ± 153 μmol/min vs. 197 ± 100 μmol/min, $P < 0.01$)) at 60 minutes, a reduction of FE-Na (2.17 ± 1.1 vs. 1.52 ± 0.82, $P < 0.05$) at 60 minutes and a reduction of GFR (106 ± 7 ml/min vs. 93 ± 14 ml/min, $P < 0.01$) at 120 minutes. Ten minutes after L-NMMA injection there was a significant increase in mean BP (81 ± 11 mm Hg vs. 90 ± 15 mm Hg, $P < 0.05$) and a decrease in HR (57 ± 6 beats/min vs. 47 ± 6 beats/min, $P < 0.01$). These changes normalized completely within 60 minutes. **Conclusion:** Despite the hypertensive effect of acute NO blocade we observed a significant reduction of renal sodium excretion, GFR and RPF. These findings suggest that NO exerts a powerful regulation of renal hemodynamics and sodium excretion in normal humans.

Combined renal effects of angiotensin II and indomethacin in patients with adult polycystic kidney disease. *C.B. Nielsen, H. Arentoft, and E.B. Pedersen, Department of Nephrology, Skejby Hospital, Aarhus, and Department of Nephrology, Aalborg Hospital, Aarhus, Denmark.* The acute effects of angiotensin II infusion without and during prostaglandin synthesis inhibition by indomethacin on renal function and plasma levels of angiotensin II (Ang II), aldosterone (Aldo), atrailt natriuretic peptide (ANP) and arginine vasopression (AVP) were studied in 17 patients with autosomal dominant polycystic kidney disease (ADPKD) and in 11 matched healthy control subjects (CS). All were investigated twice with at least 7 days apart. Ang II (1.5 ng/kg/min) was infused for two hours on both study days, whereas indomethacin only was administered on one of the two days (100 mg 12 hrs and 1 hr before clearance investigations). Glomerular filtration rate (GFR) and renal plasma flow (RPF) were measured by 125-I-iothalamate and 131-I-hippuran clearance technique. Hormones were measured by radioimmunoassays. Eleven of the 17 patients with ADPKD received antihypertensive treatment, but this was withdrawn at least two weeks prior to the examination. Ang II infusion

alone decreased GFR, RPF, urinary output ($U_{Na}V$), sodium excretion ($U_{Na}V$), fractional sodium excretion (FE_{Na}) and fractional lithium clearance (FE_{Li}) in both groups, but significantly more in the CS group. During indomethacin treatment the effects were even more pronounced: GFR (ADPKD: −10.5% vs. CS: −19.3%, $P \leq 0.01$); RPF: (ADPKD: −21.4% vs. CS: −31.8%, $P \leq 0.01$); $U_{Na}V$: (ADPKD: −35.2% vs. CS: −79.6%, $P \leq 0.01$); $U_{Na}V$ (ADPKD: −33.3% vs. CS: −80.4%, $P \leq 0.01$); FE_{Na}: (ADPKD: −23.8% vs. CS: −70.8%, $P \leq 0.01$); FE_{Li}: (ADPKD: −15.7% vs. CS: −45.5%, $P \leq 0.01$). Mean arterial blood pressure (MAP) and Ang II were increased on both days, but there was no significant difference between the changes (during Ang II and indomethacin: MAP: ADPKD: 5.4% vs. CS: 7.6%, $P = 0.32$; Ang II: ADPKD from 12.4 pmol/liter to 60.2 pmol/liter vs. CS: from 18.2 pmol/liter to 73.6 pmol/liter, $P = 0.14$). All other parameters were changed in similar ways in both groups. Our results suggest that the renal sensitivity to Ang II is decreased in patients with ADPKD, especially during prostaglandin synthesis inhibition. This might be due to reduced numbers of renal Ang II receptors in these ADPKD patients.

Organ damage in hypertension: The kidney, heart and the vascular system. *J.S. Yudkin, University College London Medical School, London, England, U.K.* Meta-analysis of the major intervention trials for hypertension has shown around a 40% reduction in stroke risk, and a 16% reduction in coronary heart disease, as a consequence of a reduction of approximately 6 mm Hg in diastolic blood pressure, achieved predominantly with thiazides and beta blockers. While this corresponds to around 65% reversibility of risk of coronary heart disease, that for stroke risk is virtually 100%. It may be calculated, however, that treating mild hypertension in a middle aged man requires 6929 person-years of treatment to prevent one stroke death, and 3345 person-years to prevent one cardiac death. The implications of these observations are that macrovascular damage is consequent upon elevation of blood pressure, but that casual blood pressure levels *per se* are poor markers of who will and will not benefit from treatment. Hypertension is associated with several phenotypes which are in turn associated with elevated cardiovascular morbidity and mortality. Microalbuminuria is a marker of renal damage in both hypertension and diabetes, and yet is found in normotensive non-diabetic subjects, in whom it is a similarly powerful predictor of vascular disease. Hyperinsulinemia clusters with several cardiovascular risk factors and may be of etiological significance in hypertension, yet is independently associated with cardiovascular disease. Left ventricular hypertrophy is a powerful prognostic marker of poor outcome in hypertension, yet correlates poorly even with ambulatory measures of blood pressure. All of these phenotypes may be associated with non-blood pressure determinants which in turn are the basis of the excess cardiovascular risk. Possible candidate antecedents for these phenotypes include genetic predisposition (ACE gene, sodium-lithium countertransport) or, for microalbuminuria and insulin resistance, endothelial dysfunction. However, recent observations on the association between these phenotypes and early growth suggest another possible antecedent. Growth retardation in late pregnancy may be associated with redistribution of blood supply from the limbs and splanchnic bed to the brain, and consequently poor vascular development in skeletal muscle, liver and kidneys. Consequent impairment in renal growth, increased peripheral resistance, and cardiac myocyte hypertrophy could result in the development of hypertension, insulin resistance, decreased nephron number, and left ventricular hypertrophy, thus explaining the coexistence of organ damage with elevated blood pressure. These hypotheses are amenable to future study.

Renal angioplasty improves renal function in the treated kidney. *G. Jensen, B-F. Zachrisson, K. Delin, R. Volkmann, and M. Aurell, Departments of Nephrology, Radiology and Clinical Physiology, Sahlgrenska University Hospital, Göteborg, Sweden.* Percutaneous transluminal renal angioplasty (PTRA) was performed in 180 renal arteries in 137 patients [30 patients with fibromuscular dysplasia (FMD) and 107 with arteriosIcerotic vascular disease (AVD)]. Total renal function was measured with ^{51}Cr-EDTA clearance and split renal function (SFR) with hippuran renography before and one year after PTRA. One year follow-up angiograms were obtained in 144 out of 180 PTRAs. Hypertension was cured or improved in 86% of FMD patients and in 64% of AVD patients with renovascular hypertension. Mean systolic and diastolic blood pressures were reduced in FMD (151 ± 21/93 ± 9 mm Hg vs. 131 ± 19/81 ± 8 mm Hg, $P < 0.001$) and AVD patients (167 ± 23/92 ± 10 mm Hg vs. 150 ± 24/84 ± 8 mm Hg, $P < 0.001$). GFR (ml/min/1.73 m^2 BSA) and SRF (%) (mean ± SD) before and one year after PTRA are shown below:

	FMD		AVD	
	Before	After	Before	After
GFR	78 ± 27	88 ± 27[a]	48 ± 24	54 ± 27[a]
GFR-SK	29 ± 15	40 ± 16[a]	21 ± 12	28 ± 13[a]
GFR-NSK	48 ± 18	46 ± 16[b]	28 ± 18	27 ± 20[b]
SRF-SK	39 ± 15	46 ± 10[a]	39 ± 19	47 ± 19[a]

Abbreviations are: SK, stenotic kidney; NSK, non-stenotic kidney, [a] $P < 0.001$; [b] NS

PTRA induces: (1) cure or improvement of hypertension in more FMD than AVD patients; (2) a significant increase in total GFR in both groups; (3) a significant increase in GFR in the treated kidney in both groups but more pronounced in the FMD group (mean changes: 11 versus 7 ml/min/1.73 m^2 BSA, respectively); and (4) no change in GFR in the non-stenotic kidney in any group. In conclusion, PTRA improves renal function of the treated kidney in both FMD and AVD patients.

The effect of a small dose of hydrochlorothiazide in hypertensive patients insufficiently controlled with enalapril monotherapy. *I. Os, A.J. Jounela, S.J. Guul, A. Haaland, A. Dyrdal, T. Risanger, and K.O. Langaker, Department of Nephrology, Ullevål Hospital, Oslo, Norway.* **Aim:** To evaluate the antihypertensive efficacy and metabolic effects of 6 mg hydrochlorothiazide (HCTZ) in hypertensive patients not adequately controlled with enalapril (E) alone. **Methods:** An open 8-week filter period with E 20 mg o.d. was followed by a randomized, placebo-controlled, double-blind 8-week period with addition of placebo (P), HCTZ 6 mg (I) or HCTZ 12.5 mg (II) in the patients with persistent DBP ≥95 mm Hg. **Results:** Of 402 patients entering the filter period, 296 patients entered the second phase. The mean reduction of DBP was significantly larger in group I and II compared to P [7.3, (CI 9.0–6.2); 7.7, (9.2–6.3); and 4.1, (5.9–2.6) mm Hg, respectively ($P < 0.001$ for I and II compared to P)]. In group II, a significantly larger increase in uric acid was observed compared with both P and I. Compared to P, both groups I and II had a small but statistically significant decrease in potassium. No differences in serum lipids were observed in the three groups. Urinary albumin excretion remained stable. Insulin/glucose ratio did not differ after addition of HCTZ, nor did HbA1c. Neither fibrinogen nor plasminogen activator inhibitor differed in the three study groups. **Conclusion:** A very low dose of 6 mg HCTZ potentiates the effect of enalapril as effectively as higher doses of HCTZ, and is well-tolerated. Addition of small doses of HCTZ (i.e. 6 and 12.5 mg) does not adversely affect glucose metabolism, serum lipids or fibrinolytic capacity in hypertensive subjects already treated with E.

Blood pressure, proteinuria and hematuria seven years after pregnancy complicated by hypertension. *E. Pettersson, H. Nisell, G. Möllerström, and N-O. Lunell, Departments of Nephrology, Gynecology and Obstetrics, Huddinge University Hospital, Huddinge, Sweden.* **Aim:** Women with hypertension (HT) during pregnancy are claimed to run an increased risk for acquiring HT later, but prevalence figures vary greatly (0–78%) in previous studies. The purpose of our study was to assess the occurrence of HT, proteinuria (P), and hematuria seven years after gestations complicated by either pregnancy induced HT (PIH, BP ≥140/90) or preeclampsia (PE, BP ≥140/90 and $P \geq 0.3$ g/24 h) and define factors that discriminate between women who remain normotensive and those who develop HT. **Study design:** All women with PIH or PE in 1986, and women with uncomplicated pregnancies who delivered the same day (controls, C) were requested to participate in a reexamination in 1993. The following investigations were done: a questionnaire, BP after 10 hours rest, body weight (BW, kg), height (m), body mass index (BMI = BW/m^2), blood and urinary samples for laboratory tests. **Results:** One hundred thirty-eight women (70% compliance) participated in the study: 49 with PIH, 45 with PE, and 44 with C. Women with PIH or PE had significantly more HT at follow-up compared with C (37% and 20% vs. 2%, $P < 0.001$), microalbuminuria (14% and 20% vs. 2%, $P < 0.05$) and higher s-Ca ($P < 0.001$), and a tendency to more hematuria ($P = 0.055$). Compared with C, BW and BMI were significantly increased in those with PIH, during index pregnancies ($P < 0.001$), and at follow-up ($P < 0.05$). Hypertension at follow-up was significantly associated with microalbuminuria ($P < 0.001$)

and multiparity at index pregnancy ($P < 0.01$). Only ten of the 28 women with HT at follow-up were aware of it at the reexamination. **Conclusion:** The risk for HT seven years after a pregnancy complicated by PIH or PE is considerably increased and associated with microalbuminuria. The fact that only 1/3 of the women with HT at follow-up were aware of this calls for an intensified control of these women at risk.

Sympathetic activity in premenopausal hypertensive women. *I. Os, G. Nordby, A. Westheim, S.E. Kjeldsen, and I. Eide, Department of Nephrology, Ullevål Hospital, Oslo, Norway.* **Aim:** To compare the sympathetic activity in never-treated hypertensive premenopausal women (HT) with age-matched normotensive women (NT) during rest and after a cold pressor test (CPT). **Methods:** All women were investigated between the 7th and 10th days of their menstrual cycle and only once each day. Blood samples for adrenaline (A), noradrenaline (NA), dopamine (D), and vasopressin (AVP) were drawn from indwelling venous (NT and HT) and arterial catheters (HT only). CPT was performed with the right hand immersed in ice water for 1 minute, and blood samples drawn 5 minutes thereafter. Blood pressures (BP) were measured with a semiautomatic oscillometric blood pressure device. **Results:** Mean BP correlated to arterial NA ($r = 0.77$, $P < 0.001$), venous NA ($r = 0.68$, $P < 0.01$), and arterial ($r = 0.53$, $P < 0.05$), but not venous A in HT. No relationship between BP and catecholamines was observed in the NT. Similarly, heart rate correlated significantly to A in HT only. No differences between NT and HT in mean concentrations of either catecholamines or AVP were observed. During CPT, HT reacted with a more pronounced increase in BP and heart rate. The significant increase in NA in HT ($P < 0.01$) after CPT did not differ significantly from the small, but not statistically significant, response in NT. **Conclusion:** The strong relationship between catecholamines and BP and heart rate in HT only suggests that in premenopausal never-treated hypertensive women, sympathoadrenal activity may be quite significantly involved in the pathogenesis of the high blood pressure, possibly through increased sensitivity.

Improved flow properties of blood after anti-hypertensive treatment with amlodipin or metoprolol. *T. Linde, B. Sandhagen, A. Hägg, C. Mörlin, and B.G. Danielson, Departments of Internal Medicine and Clinical Physiology, University Hospital, Uppsala, Sweden.* The viscosity of blood of hypertensive patients has been shown to be increased. The aim of the present study was to elucidate if anti-hypertensive treatment has any effects on the flow properties of blood. Twenty patients with previously untreated essential hypertension were included in this cross-over study and randomly allocated to four months of treatment with the calcium channel blocker amlodipin or the beta receptor blocker metoprolol. Hemorheological variables were measured with rotational viscometry.

	No treatment	On amlodipin	On metoprolol
Blood pressure *mm Hg*	161 ± 21 106 ± 7	139 ± 21 91 ± 6[b]	145 ± 24[b] 90 ± 8[b]
Hematocrit %	47 ± 3.4	45 ± 2.8[b]	44 ± 3.5[a]
Whole blood viscosity *mPa · s*	5.1 ± 0.8	4.6 ± 0.4[a]	4.6 ± 0.4[a]
Plasma viscosity *mPa · s*	1.38 ± 0.09	1.33 ± 0.08[a]	1.33 ± 0.08
Erythrocyte aggregation tendency	1.08 ± 0.08	1.05 ± 0.09	1.07 ± 0.12
Erythrocyte fluidity *1/[Pa · s]*	91 ± 12	95 ± 13	93 ± 12
S-erythropoietin *U/liter*	14 ± 6	11 ± 4[a]	11 ± 5[a]

[a] $P < 0.05$; [b] $P < 0.01$ compared with untreated hypertension

Amlodipin as well as metoprolol exert beneficial effects regarding the flow properties of blood. The decrease in whole blood viscosity was mainly caused by a decrease in hematocrit, which in turn partly might be explained by a fall in the serum concentration of erythropoietin. After amlodipin treatment the plasma viscosity decreased and the erythrocyte fluidity tended to increase, which may be beneficial to the microcirculation.

Familial clustering of raised blood pressure and insulin resistance in diabetic nephropathy. *J. Fagerudd, P-H. Groop, A-M. Teppo, and C. Grönhagen-Riska, Department of Medicine, Division of Nephrology, University of Helsinki, Finland.* **Aim:** To elucidate whether there is familial clustering of insulin resistance and other cardiovascular risk factors in parents and siblings of type 1 diabetic patients with diabetic nephropathy. **Methods:** Oral glucose tolerance test (OGTT), short insulin tolerance test (sITT), office blood pressure, near-infrared light spectroscopy for determination of lean body mass (LBM), waist/hip ration (WHR), determination of lipids and $HbA1_c$. **Results:** A total number of 200 first degree relatives (parents, siblings) of 50 type 1 diabetic patients with (AER >20 μg/min) and 50 without diabetic nephropathy (AER <20 μg/min) were studied. Diabetic patients were matched for age, sex, BMI, $HbA1_c$ and duration (>25 years). Preliminary data from 98 relatives (44 of albuminuric and 54 of normoalbuminuric patients) are presented. Relatives of albuminuric (REL_a) and normoalbuminuric patients (REL_n) showed no difference in sex distribution, BMI, WHR, LBM, fasting plasma glucose, $HbA1_c$, total cholesterol, HDL cholesterol and triglycerides, but REL_a were significantly younger (52.2 ± 1.9 vs. 56.2 ± 2.1 years). OGTT gave 13% NIDDM in REL_a and 5% NIDDM in REL_n (P = NS). REL_a had higher diastolic blood pressure (77 ± 1 vs. 74 ± 1 mm Hg, $P = 0.048$) and were less insulin sensitive compared to REL_n (KITT, 3.35 ± 0.18 vs. 3.96 ± 0.21%/min; $P = 0.031$) and this was also the tendency after excluding relatives with abnormal glucose tolerance (diastolic BP 77 ± 1.4 vs. 73 ± 1.3, $P = 0.053$; KITT 3.68 ± 0.18 vs. 4.21 ± 0.21, $P = 0.062$). **Conclusions:** Insulin resistance and raised blood pressure in family members of type 1 diabetic patients seem to be associated with an increased risk for diabetic kidney disease.

Other renal diagnoses than diabetic nephropathy are more common in non-tobacco users with IDDM. *J.G. Sörensen, G. Jaremko, and B.G. Stegmayr, Department of Internal Medicine, Division of Nephrology, University Hospital of Umea, and Division of Pathology, University Hospital, Huddinge, Sweden.* The clinical triad, of diabetes mellitus for more than 10 years, persistent proteinuria, and retinopathy, is often accepted for the diagnosis of diabetes nephropathy without further renal investigation. This study was performed to evaluate the prevalence of diabetes nephropathy (DN) or other important adjuvant renal diagnoses in patients with insulin dependent diabetes mellitus (IDDM) and renal impairment and to relate the findings to the tobacco habits of these patients. Fifty-four consecutive patients with type 1 IDDM (mean age 42.1 years, 35 men and 19 women) were admitted for renal investigation due to impaired renal function as determined by glomerular filtration rate and proteinuria. Eighteen (32%) of the patients had never used tobacco while 36 (68%) had or were tobacco users (smokers or snuff). Renal diagnoses were verified by renal biopsy as: isolated DN findings, (N = 43, 80%), DN with additional glomerulonephritis (N = 9, 17%), DN in combination with interstitial nephritis (N = 2, 4%). Among the 43 patients with isolated diabetic nephropathy, 34 (63%) were former or current tobacco users. In the group of patients with other renal diagnoses (N = 11, 20%) two patients (4%) were former or current tobacco users while nine (17%) had never used tobacco. In regard to the material, tobacco users had a significantly greater prevalence of isolated diabetic nephropathy than the non-tobacco users (Fisher's exact test: $P = 0.0003$, relative risk 1.889 (1.182–3.019), odds ratio 17.0 (3.107–93.024).

Three new mutations in the vasopressin-neurophysin II gene are associated with familial neurogenic diabetes insipidus. *S. Rittig, C. Siggaard, I. Os, N. Gregersen, and E.B. Pedersen, Department of Medicine and Nephrology C, and Center of Medical Molecular Biology, Skejby Hospital, University Hospital, Aarhus, Denmark, Department of Medicine, Oslo University Hospital, Oslo, Norway.* Familial neurogenic diabetes insipidus (FNDI) is a rare autosomal dominant disorder due to a deficient pituitary secretion of arginine vasopressin (AVP) and characterized by chronic polyuria and polydipsia. The deficiency of AVP secretion develops during early childhood, and there is evidence that the deficiency is caused by degeneration of magnocellular neurons in the supraoptic and paraventricular nuclei. Since 1991 eight different mutations in exon 1 or 2 of the vasopressin-neurophysin II (VP-NPII) gene have been identified. In the present study three other kindreds [two Danish (Kr, Jo) and one Norwegian (Aa)] with clinical evidence of FNDI were investigated in order to identify the genetic defect responsible for the disease. A sequencing method was used for sequenase dye-terminator sequencing directly on single-stranded PCR-amplified genomic DNA. With biotinylation of one of the flanking primers around each exon (1–3), the exons were amplified separately by PCR and subsequently purified through incubation and fixation with Dynabeads®. Finally, the purified single-stranded PCR

product was sequenced in both directions depending on the sequencing primer used. The results showed that each of the 3 families had a new and so far unreported single base mutation in the VP-NPII gene. One family (Jo) with 10 members (5 affected) had a mutation ($T_{1839} \rightarrow C$ predicting $Leu_{50} \rightarrow Pro$) located in the highly preserved part of NPII in exon 2. This mutation, which is likely to interfere with the conformation of the AVP binding pocket, co-segregated perfectly with the disease phenotype in this family. The Aa kindred had a nonsense mutation ($C_{1873} \rightarrow A$ predicting $Cys_{61} \rightarrow$ Stop) in the preserved part of exon 2. The Kr kindred also had a nonsense mutation ($C_{2094} \rightarrow A$ predicting $Cys_{79} \rightarrow$ Stop) but located in the variable part of NPII in exon 3. These non-sense mutations could either interfere with translation or result in a truncated NPII peptide. In summary, we have identified 3 new disease causing mutations that all are likely to induce conformational changes of the three-dimensional NPII structure that could impair the normal intracellular processing of the pro-hormone.

Relationship between hemorheological factors and insulin sensitivity in normotensive and hypertensive women. *G. Nordby, A. Moan, S.E. Kjeldsen, and I. Os, Department of Internal Medicine, Ullevål Hospital, Oslo, Norway.* **Aim:** To test a possible relationship between hemorheological factors such as hematocrit and whole blood viscosity and insulin sensitivity index (GDR/I) in hypertensive (HT) and normotensive (NT) premenopausal women. **Methods:** HT (BP 149 ± 5/99 ± 2 mm Hg, $N = 14$) and NT (BP 128 ± 4/81 ± 2, $N = 12$). Lean women, matched for age, weight and body mass index (BMI) were studied with euglycemic glucose clamp technique and insulin sensitivity index (glucose disposal rate [GDR/insulin (I)] determined. Whole blood viscosity (WBV) was calculated at different shear rates (SR). **Results:** GDR/I was similar in HT (7.3 ± 0.8 a.u.) and NT (7.6 ± 0.8 a.u.). WBV did not differ between HT and NT at any SR (SR 5.2 sec^{-1}: 7.5 ± 0.4 vs. 8.0 ± 0.3, NS). Statistically significant negative correlations were observed between GDR/I and WBV at both high ($r = -0.49$, $P < 0.01$) and low ($r = -0.50$, $P < 0.01$) SR. In multiple-regression analysis, WBV, BMI, systolic and diastolic blood pressure accounted for 39% of the variation in GDR/I, but only WBV was an independent explanatory variable for GDR/I. **Conclusions:** These associations between calculated whole blood viscosity and insulin sensitivity index suggest hemorheological and therefore indirectly hemodynamic factors as correlates to insulin sensitivity.

Does microalbuminuria determine insulin resistance in hypertension? *T.G. Jenssen, I. Toft, and K.H. Bønaa, University of Tromsø, Tromsø, Norway.* Type II diabetics with microalbuminuria (MA) tend to have a more developed degree of insulin resistance than those without MA. This suggests that MA in diabetes describes a mechanism which by itself contributes to insulin resistance. **Aim:** To see if MA determines a more pronounced degree of insulin resistance in hypertensive (HT) persons without diabetes as well. **Methods:** Twenty-six HT persons with (MA+) and 33 age, weight, and sex matched HT persons without MA (MA−) underwent an oral glucose tolerance test (OGTT) and a 180 minute hyperglycemic (HG) clamp. Half of them also underwent a hyperinsulinemic euglycemic (EG) clamp. **Results:** The two groups (MA+ vs. MA−) did not differ significantly in systolic (157 ± 2 vs. 150 ± 2) and diastolic (99.0 ± 1.0 vs. 98 ± 1.0) blood pressures (mm Hg). Fasting plasma glucose (5.8 ± 0.2 vs. 5.7 ± 0.1 mM) and insulin (11.7 ± 2.1 vs. 11.9 ± 1.9 μU/ml) were identical too. The OGTT elicited similar plasma glucose responses in the MA+ and MA− group, and the incremental areas under the insulin curves were 181.6 ± 22.7 and 192.3 ± 24.3, respectively (P = NS). The insulin sensitivity index as measured from the HG clamp was 0.16 ± 0.02 in the MA+ group and 0.17 ± 0.02 in the MA− group (P = NS). Corresponding findings were obtained with the EG clamp, with a correlation factor of $r = 0.69$ ($P < 0.0001$) between the two clamp techniques. **Conclusion:** Microalbuminuria is not an independent marker of insulin resistance in hypertensive persons without diabetes.

Individual strategies to achieve maximum treatment dose in automated peritoneal dialysis (APD). *T-E. Widerøe, K. Aasarød, L. Smeby, K. Dahl, and S. Jørstad, Department of Nephrology, University of Trondheim, Norway, and Gambro AB, Lund, Sweden.* The purpose was to define strategies for maximal individual solute mass transfer, and design a nomogram where these informations easily can be depicted. A physiological model to simulate intraperitoneal (Ip) solute and fluid kinetic was used. Clinical values used: (1) equilibration test; (2) catheter function: 135–200 ml/min; (3) fill volume: 1–2.5 l, (4) treatment time: 9–10 hr; (5) dialysate volume: 10–40. These parametres were related to mean treatment clearance (Cl) for urea. Tidal PD (TPD) and IPD were compared and related to CAPD. **Results:** (1) Upper possible Cl (l/week) for CAPD (8 l/day) exceeded that of IPD/TPD (10 × 7 hr/week), 2) IPD gave higher Cl than TPD for volumes <30–40 l, 3). Changes in peritoneal membrane permeability gave up to 3 liters/day difference in Cl, (4) Shortening the inflow/outflow time for TPD from 7/8 to 5/6 min increased Cl by 15% when using 25 l dialysate; (5) Changing fill volume from 1 to 2.5 l and using 16 liters dialysate, increased Cl by 35%. From one measured Cl, the nomogram defines the individual permeability and Cl by any cycling time for TPD and IPD. The calculated results where controlled by measurements from a prospective cross over study including CAPD, CCPD and TPD in six patients. **Conclusion:** Calculated and measured values correlated significantly. For different permeabilities of the peritoneal membrane and by stable catheter function, IPD is more effective than TPD, by dialysate flows below 30–40 ml/min. The treatment efficacy is heavily influenced by catheter function and by the individual peritoneal membrane. Useless consumption of high dialysate volumes is suggested.

Different approach to dry body weight (BW) determination—different effect on blood pressure (BP) control in chronic hemodialysis (HD) patients. *K.S. Katzarski, B. Charra, J. Bergström, and G. Laurent, Department of Renal Medicine Huddinge University Hospital, Sweden, and Centre de Rein Artificiel de Tassin, France.* The aim of this study was to evaluate the importance of volume status on BP control in chronic HD patients. Extracellular fluid volume (ECV) and 48 hour BP monitoring (BP_{48}) of two groups (G) of HD patients were compared: G1: 12 hypertensive patients from Huddinge and G2 30 randomly selected patients from Tassin (G2). ECV of the patients was compared also to 30 healthy. G1 was treated with 4 hr–4.5 hr HD procedure and 1 or more antihypertensive drugs (AD), while G2 ($N = 22$) was treated with 8 hr HD procedure or 5 hr procedure ($N = 8$) after attaining a reasonable dry BW which includes a good BP control with no use of AD. Pre- and post-HD ECV was measured by multifrequency bioimpedance (Xitron, USA), calculated using the Cole-Cole model and Hanai equation and presented as % of BW. BP_{48} was performed by the SpaceLabs 90207 device. ECV of the healthy subjects was 25.6 ± 3.6%. Their casual MAP was 88 ± 6 mm Hg.

	G1	G2	P
Age	52 ± 15	64 ± 11	<0.01
BMI	22.2 ± 3.3	24.0 ± 4.6	NS
% ECV pre-HD	29.7 ± 4.5	26.4 ± 3.2	<0.01
% ECV post-HD	26.7 ± 2.7	23.7 ± 3.0	<0.0025
MAP	117 ± 13	80 ± 13	<0.0001

No differences in ECV and BP_{48} of 8 hr and 5 hr patients in G2 were found. When ECV of 5 patients from G1 was gradually decreased to 24.7 ± 1.7% in 3 months, their MAP decreased from 137 ± 15 to 94 ± 16 mm Hg and AD were discontinued. In conclusion, maintaining a reasonable dry BW is essential for BP control, but whether a lower than normal ECV is necessary needs to be studied.

Angioaccess for hemodialysis during a 15 year period. *C. Eriksson, L. Brunes, A. Lindhagen, and J. Ahlmén, Departments of Nephrology and Surgery, Central Hospital, Skövde, Sweden.* A reliable angioaccess (A) is still essential for chronic hemodialysis treatment. We have followed the surgical development of A in our hemodialysis population over the last 15 years. **Materials:** Two hundred fifty-eight patients (163 males and 95 females) with a mean age of 62 (range 15–90) years, who started on hemodialysis in the county of Skaraborg between 1979 and 1994, were studied. Four hundred twenty-eight A were constructed, and 114 were excluded, 91 as non-permanent A and 23 as unclassified. Three hundred fourteen A were studied. **Results:** Out of 314 A, 276 were A-V fistulas of the forearm, 27 of the elbow, 6 of the overarm, and 5 were grafts. Two hundred five A were first accesses, 69 second, 25 third, and 1 patient had 6 angioaccesses. In the entire material the 5 year patency was 61%. An improved patency rate was seen over time. The last 5 year period showed a 5 year patency of 71%. The result was influenced by the number of

surgeons involved. Surgical technique influenced the result. The side to side anastomosis showed the best patency rate. Patient age did not affect A patency. Systemic diseases showed worse results than primary renal diseases. **Conclusion:** A few interested surgeons with a stable technique is the most important factor for improved angioaccess patency. The type of anastomosis and the number of patients with systemic diseases are also important.

Calcium carbonate versus aluminum hydroxide as phosphate binder in hemodialysis patients. A randomized prospective study. *K.P. Nordal, H.P. Aarseth, J. Halse, E. Dahl, H. Langberg, and P. Fauchald, The National Hospital and Ullevål Hospital, Oslo, Norway.* **Aims:** To study the effects of $CaCO_3$ and $Al(OH)_2$ used as phosphate binders on serum and bone Al, bone histology, and bone metabolism. **Methods:** Twenty-six patients on hemodialysis treatment were included. None was using calcitriol. The Ca^{++} cone in the dialysate was 1.75 mmol/liter. Eight patients did not complete the study. In the remaining 18 patients serum P was kept below 1.8 mmol/liter by individually adjusted doses of phosphate binder. Blood samples were taken regularly during the study and a bone biopsy obtained at start and end. **Results:** According to initial randomization 12 patients received $CaCO_3$ and 6 $Al(OH)_2$. Because of hypercalcemia (serum Ca >2.7 mmol/liter), the $CaCO_3$ doses had to be reduced and $Al(OH)_2$ supplemented in 3 patients. These 3 patients are included in the $Al(OH)_2$ group during the statistical analysis. The area under the curve (AUC) for serum P, Ca, and PTH was similar in the two groups, while the AUC for serum Al and ALP was significantly higher in the $Al(OH)_2$ than in the $CaCO_3$ group ($P = 0.002$ and 0.025, respectively). Al stained bone surfaces tended to increase in the $Al(OH)_2$ and decrease in the $CaCO_3$ during the study, but the difference did not reach statistical significance ($P = 0.13$). The other bone histomorphometric indices were similar in the two groups both at start and end of the study. **Conclusion:** Both $CaCO_3$ and $Al(OH)_2$ are well tolerated as phosphate binders in hemodialysis patients. $CaCO_3$ may lead to hypercalcemia, while $Al(OH)_2$ increases serum Al and tends to increase bone Al.

Cefuroxime i.p and i.v. reduces post-operative peritonitis in CAPD. *A.M. Wikdahl, U. Engman, B.G. Stegmayr, and J.G. Sörenssen, Department of Internal Medicine, University Hospital, Umea, Sweden.* When a Tenckhoff catheter (TeC) is inserted in a patient starting CAPD there is always a risk for peritonitis, and the bacteria most likely to be the agents are *S. aureus* and *S. epidermidis.* At our center dialysis is started immediately after the TeC operation without any period of rest of the wound or peritoneal cavity. The aim was to evaluate if postoperative peritonitis could be reduced by prophylactic antibiotic therapy. **Materials and methods:** During 27 months 38 patients consecutively entering the CAPD program were included in the study (11 women and 27 men, mean age 57 years, range 33–84) and randomized either to prophylaxis with 1.5 g of cefuroxime i.v. preoperatively and 250 mg intraperitoneally in the first dialysis bag (Group I: 18 patients, mean age 56 years, females 6, diabetes mellitus 6) or without antibiotic prophylaxis (Group II: 20 patients, mean age 58 years, females 5, diabetes mellitus 8). All insertions were performed in an operation theater by the same surgeons using the same technique. **Results:** In Group I none of the 18 patients received peritonitis within the first 10 days after TeC implantation and start of dialysis, while in group II 6 of 20 patients suffered from peritonitis ($P = 0.021$, Fishers test). We conclude that prophylactic cefuroxime i.v. pre-operatively and i.p. perioperatively and post-operatively may reduce the risk for peritonitis associated with the insertion of the Tenckhoff catheter.

Present status and future trends in transplantation immunology. *E. Thorsby, Institute of Transplantation Immunology, The National Hospital, Oslo, Norway.* HLA matched kidneys induce less severe and less frequent rejection episodes than HLA mismatched kidneys, which results in better graft survival in the former case, both short-term and long-term. This is clearly established for kidneys both from living and cadaveric donors. In particular, matching for HLA class II molecules appears to be important. Recent knowledge of the biological function of HLA molecules provides an explanation. The HLA molecules are informers for T cells about intracellular proteins. HLA class I molecules (A, B and C) mainly present peptide fragments from endogenously synthesized proteins to $CD8^+$ T cells, while class II molecules (DR, DQ and DP) mainly present peptide fragments from exogenous or membrane bound proteins to $CD4^+$ T cells. The T cell receptor (TCR) thus recognizes peptide/HLA complexes. The HLA molecules are extremely polymorphic and different variants bind and present different sets of peptides to T cells. Since T cells are largely tolerant to peptides from self proteins, a T cell response will normally be induced only to peptides from foreign proteins presented by self HLA molecules, i.e. foreign peptide/HLA complexes. Following transplantation from an allogeneic donor, the T cells of the recipient will indirectly or directly recognize foreign peptide/HLA complexes. Indirect allorecognition is a result of foreign allogeneic cell-proteins being taken up by recipient antigen presenting cells (APC). Peptide fragments from these allogeneic proteins may then be presented by recipient class II molecules to recipient $CD4^+$ T cells. Since the foreign HLA molecules themselves are an important source of foreign allogeneic cell-proteins, more T cells will be activated via indirect allorecognition when the donor carries HLA molecules different from those of the recipient than when they are HLA identical. Direct allorecognition is the result of direct presentation of peptides from foreign allogeneic cell-proteins by the class I and II molecules of the allogeneic cells themselves, to recipient $CD8^+$ and $CD4^+$ T cells, respectively. Since different HLA molecules bind different sets of peptides, more foreign peptide/HLA complexes will be directly presented to recipient T cells when the HLA molecules of the donor are different from those of the recipient than when they are HLA identical, leading to more T cells being activated in the former than in the latter case. Together, this leads to stronger allograft immune responses when donor and recipient are mismatched for HLA than when they are matched. To obtain prolonged graft survival with less doses of immunosuppressive drugs required, and therefore also reducing the need for re-transplantation (and thus saving kidneys), all efforts should be made to secure an HLA well-matched kidney. This possibility should be optimally utilized since the technology is still not here to induce specific tolerance to the many foreign peptide/HLA complexes in an allogeneic kidney, or to overcome the more severe immunological barrier which exists in xenotransplantation.

Nasal calcitonin reduces bone loss in renal transplant recipients. *K.P. Nordal, J. Halse, J. Kronborg, E. Dahl, G. Sødal, and P. Fauchald, Medical and Surgical Departments B, Rikshospitalet and Betanien Medical Laboratory, Oslo, Norway.* Bone loss after kidney transplantation (Tx) may lead to severe skeletal problems. Since most kidney recipients have high turnover bone disease at Tx, we studied the effect of nasal calcitonin on bone mineral density (BMD) the first year after Tx. **Methods:** Sixty-two patients received in a double-blind fashion either nasal calcitonin 200 U/day ($N = 32$) or placebo ($N = 30$) for 12 months after Tx. All were receiving standard protocol treatment for kidney transplant recipients (low dose steroids, cyclosporine A, and azathioprine). BMD of the lumbar spine and hip (Lunar DPX-alpha) as well as BMD at distal 1/3 site of the forearm (SPA, Crafon bone scanner) were measured. **Results:** There were significant reductions in DMD of the lumbar spine and forearm in both groups after 12 months. However, BMD L2–4 was reduced by 2.3% in the calcitonin treated patients, significantly different from the 4.4% observed in the placebo group ($P = 0.02$). In the forearm the relative reductions were 4.7 and 3.6% in the calcitonin and placebo treated groups, respectively. In the hip (neck) no significant reduction in BMD was seen in calcitonin treated patients (1%, P = NS, while a 3.2% ($P = 0.006$) reduction was seen in the placebo group. However, no group difference was observed ($P = 0.10$). **Conclusion:** Nasal calcitonin 200 U/day reduces bone loss in the lumbar spine and hip in kidney recipients during the first year after Tx.

Unrelated living donors in kidney transplantation. *A. Foss, H.A. Gjertsen, T. Leivestad, P. Fauchald, Ø. Bentdal, P. Pfeffer, B. Lien, O. Øyen, D. Albrechtsen, I.B. Brekke, O. Søreide, and G. Sødal, Surgical Department B and Institute of Transplantation Immunology, The National Hospital, Oslo, Norway.* From 1983 through 1993 a total of 1645 patients received a first kidney transplant in Norway. Grafts were procured from cadaveric donors (CD) in 881 cases (54%) and from living donors (LD) in 764 cases (46%). Of the 764 LD treated patients, 116 (15%) received a graft from an HLA-identical donor, 508 (66%) from a related donor mismatched for 1 HLA haplotype, 50 (7%) from a related donor mismatched for 2 haplotypes, and 90 (12%) received grafts from unrelated living donors. The aim of this study was to evaluate the graft survival of recipients of grafts from unrelated LDs versus related LDs and CDs. Survival rates

were calculated with the Kaplan-Meier method and curves were compared employing the Mantel-Haenszel test. Patient death with functioning graft was considered as graft loss. The 1 and 5 year graft survivals for related LD recipients receiving grafts mismatched for one or two HLA haplotypes were 91% and 74%, respectively. For the unrelated LD recipients the graft survival was 83% (1 year) and 68% (5 years), and for the CD recipients it was 78% and 59%. The graft survivals of recipients of HLA identical grafts were 99% and 94%. The difference in graft survival of related LD recipients, receiving one or two haplotype mismatched grafts, compared with unrelated LD recipients did not reach statistical significance. The graft survival in unrelated LD recipients was significantly better than for CD recipients ($P < 0.05$). Superior graft survival was observed in recipients of HLA identical grafts ($P < 0.01$). In conclusion, the study shows that the graft survival of recipients of grafts from unrelated LD recipients is good and better than CD transplantations.

Kidney transplantation to patients with IgA nephropathy. *P. Freese, G. Nordén, C. Svalander, and G. Nyberg, Transplant Unit, Sahlgrenska University Hospital, Göteborg, Sweden.* The outcome of kidney transplantation (Tx) in patients with IgA-nephropathy (IgA-NP) was evaluated retrospectively with the focus on rejection and recurrence. Patients with established IgA-NP were found to constitute 7.3% of 1000 consecutive patients who received kidney transplants in Göteborg from 1985 to 1993. Sixty-nine patients received first transplants, 46% from living donors (LD), and 19% were predialytic. Seventy-nine percent were men. Mean age (±SD) was 26 ± 10 years when symptoms first appeared, and 36 ± 11 years at the time of Tx. The patients were followed for 1–10 years, median 49 months. Biopsies were obtained only on clinical indications. **Results:** After one year, all patients but one were alive (99%), with 60 (87%) having a functioning graft. The actual 3-year survival rates were 100% and 78%, respectively ($N = 50$). The proportion of patients treated for rejection episodes during the first year after Tx was 57%, and the mean number of days with such treatment 5.3 ± 7.6, not significantly different from our average 56% and 4.8 ± 6.2, respectively. At the time of the final evaluation, 18/69 grafts were lost. Rejection caused 9 losses, 5 within 6 months and 4 later. Recurrence of IgA-NP was verified in 8 grafts and caused 5 graft losses; one after 6 months, the others after 3–4 years. All 8 grafts with recurrence were from LD ($P = 0.015$ vs. patients without recurrence), including one from an identical twin. IgA-NP was also found in 5 grafts of patients with renal failure of unknown etiology in the cohort ($N = 1000$). These grafts were from non-related donors. **Conclusions:** IgA-NP was the cause of uremia in probably more than 10% of the transplant population. Short-term survival was excellent, but there was no support for the hypothesis that this was due to reduced risks of rejection. In the long-term, recurrence caused as many graft losses as rejection. The risk of recurrence was increased among recipients of kidneys from living related donors.

Fluvastatin lowers atherogenic lipids safely in renal transplanted patients. *H. Holdaas, K. Dahl, A. Hartmann, J. Stenstrøm, K. Aasarød, B. Draganov, K. Lund, K. Nordal, K.J. Berg, M. Borge, T.C. Eide, and P. Fauchald, National Hospital, Oslo, and University Hospital, Trondheim, Norway.* Lipophilic HMG CoA reductase inhibitors have been associated with rhabdomyolysis in cyclosporine A (CsA) treated patients. Our study examined the safety and efficacy of the hydrophilic HMG CoA reductase inhibitor fluvastatin in CsA treated renal transplanted patients. After a 4-week placebo period, fluvastatin was given in a dose of 20 mg daily for 12 weeks and then increased to 20 mg twice daily for the next 36 weeks.

	Placebo (15)	Week 12 (15) Fluvastatin 20 mg × 1	Week 48 (12) Fluvastatin 20 mg × 2
Total cholesterol *mmol/liter*	8.1 ± 0.3	6.7 ± 0.3[c]	6.0 ± 0.3[cd]
LDL cholesterol *mmol/liter*	5.5 ± 0.3	4.2 ± 0.3[c]	3.6 ± 0.2[cd]
HDL cholesterol *mmol/liter*	1.5 ± 0.1	1.5 ± 0.1	1.7 ± 0.1[b]
Triglycerides *mmol/liter*	2.6 ± 0.4	2.1 ± 0.3[a]	1.9 ± 0.2[b]
Creatinine kinase *U/liter*	98 ± 11	111 ± 13	106 ± 13
CsA concentration *μg/liter*	154 ± 12	146 ± 10	148 ± 9
Creatinine *μmol/liter*	170 ± 16	176 ± 18	176 ± 18

[a] $P < 0.05$; [b] $P < 0.01$; [c] $P < 0.001$ vs. placebo; [d] $P < 0.01$ vs. week 12

Fluvastatin reduced T-chol, LDL-chol and TG. HLD-chol was increased during 40 mg fluvastatin. Fluvastatin did not affect CsA concentration. Creatinine kinase remained unchanged. The hydrophilic HMG CoA reductase inhibitor, fluvastatin, appears to be effective and safe in lowering atherogenic lipids in renal transplanted patients.

Immunoadsorption in the treatment of acute vascular rejection after renal transplantation. *G. Sterner, D. Bucin, H. Ekberg, M.O. Persson, N.H. Persson, and P. Swedenborg, Department of Vascular and Renal Diseases, Malmö University Hospital, Malmö; Blood Centre and Department of Nephrology, University Hospital, Lund, Sweden.* Histologically proven vascular rejection and the presence of cytotoxic donor reactive antibodies are associated with early renal transplant dysfunction. An effective antibody treatment may reverse this type of rejection. **Material:** To 12 patients, with deteriorating graft function in spite of intensive antirejection treatment, immunoadsorption (IA) using protein A (Citem 10^R) was given. The mean number of IA for each patient was 3.6, and approximately 3 plasma volumes were processed at each treatment. Ten patients developed histological signs of vascular rejection. In the majority of cases treatment was supplemented with plasma exchange and ATG or OKT 3 and followed by administration of high dose IgG. All patients were sensitized before transplantation (previous transplantation and/or blood transfusions) and 10 had pre-transplant panel reactive antibodies. No donor reactive antibodies (DRA) were found at transplantation. A new test was undertaken in 11 cases before start of IA and 9 were found to be positive. **Results:** In five patients renal function recovered and they have been followed for a minimum of 8 months up to 6 years. Of the remainder, one patient demonstrated 3 1/2 months graft survival after IA treatment while in the other 6 patients graftectomy was performed within 1 month. DRA titers turned negative in the group of patients with recovering renal function, but were unaffected in those with early graft failure. **Conclusion:** In this retrospective study the use of IA in acute vascular rejection after renal transplantation was successful in approximately 50% of the patients. The results allow further use of IA, but a prospective study to evaluate the treatment is desirable.

Epitope specificity of anti-GBM antibodies demonstrated with synthetic peptides. *T. Hellmark, C. Brunmark, J. Trojnar, and J. Wieslander, Department of Nephrology, Lund, and Ferring AB, Malmö, Sweden.* Autoantibodies to the non-collagenous domain (NC1) of type IV collagen are found in patients with anti-GBM nephritis. The antigen has been localized to the α3(IV) chain. However, autoantibodies to the other chains are also found and in 1 patient with a mild glomerulonephritis we have found antibodies to the α1(IV) chain only. In this study we have compared the antibodies from patients with Goodpasture syndrome and the antibodies from the patient with the α1(IV) antibodies and determined the epitope for then antibodies. We have used antigens purified from bovine tissues, recombinant protein and synthetic peptides. The specificity of the antibodies to the different α(IV) chains has been investigated with ELISA and immunoblotting. The reactivity was further investigated by overlapping synthetic peptides, covering the complete NC1 domains of the α1(IV) and the α3(IV) chains. The Goodpasture antibodies did not recognize any of the peptides, which suggests a complicated conformational epitope. The antibodies from a patient with anti-α1(IV) antibodies only was found to react with a peptide consisting of the last 20 C-terminal amino acid residues on the α1(IV) chain. We have localized the epitope to the 4 last peptides in the C-terminal end of the α1(IV) chain by using glycine substitution. The sequence is 1754-MRRT-NH_2, of which the 2 arginine residues are essential. These 4 amino acids are also determined to be the smallest peptide that could inhibit the binding of the autoantibodies to the α1(IV) chain. The α1(IV) chain has a very large sequence analogy with the α3(IV) and the α5(IV) chains, but no crossreaction was found. The results show that the specificity of the anti-GBM antibodies is of great importance for the development of disease and the importance of an analyzing method that only detects the pathogenic antibodies.

Evaluation of a rapid screening test for ANCA and anti-GBM. *K. Westman, P. Bygren, I. Eilert, A. Wiik, and J. Wieslander, Department of Nephrology, University of Lund, Statens Seruminstitute, Copenhagen and Wieslab AB, Lund, Sweden.* Reno-pulmonary syndrome is an etiologically heterogeneous group of diseases. It is a medical emergency with a high mortality unless treated. To be effective, therapy must be instituted early

in the course of the disease. Normally more than 80% of the patients presenting with these signs have one of three antibodies, that is anti-GBM (the Goodpasture antibody), PR3-ANCA or MPO-ANCA. A rapid screening assay for these three autoantibodies was developed. The total assay can be performed in 30 minutes. One thousand sixty samples from patients suspected of reno-pulmonary syndrome or RPGN were assayed using the rapid screening test; 142 (13%) were positive in either test. Seven samples (0.7%) were unspecific, that is they reacted equally with all three antigens as well as the control antigen (HSA). Nineteen specimens (2%) contained anti-GBM antibodies, 60 (6%) had PR3-ANCA, and 73 (7%) had MPO-ANCA while 10 were double positive (8 anti-GBM-MPO, 1 anti-GBM-PR3, 1 PR3-MPO). The risk that one could miss some ANCA positive samples by only using ELISA was studied. One hundred six samples were analyzed by IIF for ANCA: 84 were negative, 10 had ANA, 4 cANCA and 7 pANCA. Eleven samples (10%) were thus positive in IIF but negative in ELISA. Western blotting with alpha granule extracts was performed on the 11 samples and the clinical data of the patients obtained. None of the samples showed bands on blotting migrating as PR3 or MPO, even though several samples stained one or more bands on the blot. The ELISA thus detects the true antibodies to PR3 and MPO while IIF picks up some additional specificities. The patient data indicate that the sera were derived from a spectrum of diseases ranging from arthritis to vasculitis. This indicates that the rapid assay has a high diagnostic specificity as well as a high sensitivity and is useful in the diagnostic workup of patients suspected of having RPGN or reno-pulmonary syndromes.

A relational database for the correlative assessment of histopathological and clinical findings in renal disease. *U. Strömbom, C. Svalander, J. Ahlmén, and G. Westberg, Department of Nephrology, Central Hospital, Skövde, and Departments of Pathology and Nephrology, Sahlgrenska Hospital, Göteborg, Sweden.* Extensive and detailed information on historical and current clinical events combined with detailed histopathological information may help advance knowledge and prognostic and therapeutic possibilities in renal disease. In recent years relational databases have been arranged to receive data of this kind. Presently we have constructed such a database register (using 4th Dimension 3.2) for renal patients being subjected to renal biopsy, including background information and an extensive scheme for entering specific histopathological and immunohistochemical findings. The register also contains input follow-up data for one year, preliminarily. The output summarizing possibilities are predetermined and rather limited, as further statistic processing should be performed within appropriate applications after export of data. When building such a register one strategic issue appears to be simple yet adequate registration of the onset of disease in relation to clinical measures and renal biopsy, in particular since, for example, nephritides are clearly different in elapsed time to biopsy, also within the same clinical diagnosis. Another question is the optimal amount of information. The present extensive database will be demonstrated on a computer.

Pathogenesis of membranoproliferative glomerulonephritis (MPGN) type II in porcine factor H deficiency. *J.H. Jansen, K. Høgåsen, A.M. Grøndahl, T.E. Mollnes, and M. Harboe, Department of Morphology, Genetics and Aquatic Biology, Department of Large Animal Clinical Sciences, Norwegian College of Veterinary Medicine; Institute of Immunology and Rheumatology, University of Oslo; University of Tromsø, Tromsø, Norway.* We have recently described hereditary porcine MPGN type II. It was inherited as an autosomal recessive disorder with complete penetrance, caused by deficiency of the soluble complement regulatory protein factor H. Affected piglets were hypocomplementemic with low plasma complement C3 and high plasma terminal complement complex (TCC) concentrations. They had normal perinatal viability and performed well compared with unaffected littermates during the first few weeks of life, until a sudden onset of clinical signs including anorexia, pallor, and lethargy coinciding with an abrupt elevation in serum urea and creatinine. All affected piglets eventually died of uremia within 11 weeks (median survival 37 days). Autopsy findings included enlarged, pale and firm kidneys with fine granular surfaces. Light microscopy revealed salient glomerular mesangial cell proliferation with capillary wall thickening, frequently combined with capsular exudation and cellular crescent formation. No extrarenal lesions were observed except from secondary uremic changes such as anemia and gastric ulceration. Conspicuously thickened glomerular basement membranes with intramembranous electron dense deposits were disclosed at electron microscopy. Immunofluorescence microscopy revealed massive glomerular deposits of C3 and TCC in a pseudolinear to granular pattern along the glomerular capillary walls, but no immunoglobulin deposition. Delicate linear complement deposition was observed already in 35 days preterm fetal glomeruli, whereas intramembranous dense deposits and cell proliferation were never observed before 4 days of birth. Our observations indicate that glomerular complement activation is the triggering pathogenetic event in the development of MPGN type II.

Expression of normal and mutant cDNA encoding the vasopressin-neurophysin II precursor in mammalian cell lines. *C. Siggaard, S. Rittig, T.G. Jensen, G.L. Robertsen, L. Bolund, N. Gregersen, and E.B. Pedersen, Department of Medicine C and Center of Medical Molecular Biology, Skejby University Hospital, Institute of Human Genetics, Aarhus University, Aarhus, Denmark, and Department of Medicine, Northwestern University Medical School, Chicago, Illinois, USA.* Familial neurogenic diabetes insipidus (FNDI) is a rare, autosomal dominant disease characterized by polyuria and a deficient neurosecretion of antidiuretic hormone (AVP). Several different mutations in the vasopressin-neurophysin II gene (AVP-NPII) have been shown to be associated with FNDI. This study aimed to test the hypothesis that mutations in the AVP-NPII gene result in intracellular accumulation of abnormally folded precursor protein that subsequently leads to cell death. We developed an expression model with transfection of normal and mutant cDNA containing the most frequently found mutation in FNDI ($G_{279} \rightarrow A$ predicting Ala_{-1} to Thr) into COS-7 cells and two different neuronal cell lines (human HiB5 and mouse NT2). Expression of this -1 signal peptide (SP) mutation in COS-7 cells showed that wild-type cells are capable of producing and secreting AVP and that the cells transfected with mutant cDNA secreted much less AVP into the medium (17-fold reduction). Immunofluorescence showed that the staining of AVP and NPII in mutant cells is diffuse and not concentrated in granules as in most wild-type cells. Western blotting indicated that the mutation inhibited the cleavage of the signal peptide. When the proteins were stably expressed in HiB5 and NT2 cells which can be induced to differentiate into post-mitotic neurons, the same abnormalities in secretory capacity and cellular morphology were found. In conclusion, the -1 SP mutation in the AVP-NPII gene results in reduced capacity for vasopressin secretion in both neuronal and non-neuronal cell systems and that abnormally processed NPII immunoreactive protein accumulates intracellularly. The results support the hypothesis that disease causing AVP-NPII mutations direct the production of an abnormal AVP-NPII precursor which cannot be processed correctly and subsequently results in neuronal cell death.

Taurine and water channels are colocalized in renal tubule cells and other tissues: Immunocytochemical studies in rat. *M. Amiry-Moghaddam, E.A. Nagelhus, S. Nielsen, and O.P. Ottersen, Department of Anatomy, University of Oslo, Norway; Department of Cell Biology, University of Aarhus, Aarhus, Denmark.* Taurine is thought to function as an organic osmolyte in kidney and brain. Using lightmicroscopic and quantitative electronmicroscopic immunogold cytochemistry, we have shown that taurine is heterogeneously distributed among different populations of tubule cells in the rat kidney, and that the cellular level of taurine varies independently of the external osmotic pressure. The common feature of the cells enriched in taurine is their high water fluxing capacity. The tubule cells with a high content of aquaporin-1 (proximal tubules and descending thin limbs) and aquaporin-2 (collecting ducts) displayed a high content of taurine, and the cells with no water channels (ascending thin limbs and thick ascending limbs) were virtually devoid of taurine. We investigated whether taurine and water channels are similarly colocalized in extrarenal tissues. Specific antisera against taurine revealed high levels of this amino acid in red blood cells, excretory duct epithelia in pancreas, biliary duct epithelia in liver, corneal endothelia, capillary endothelia in several organs including brain and kidney, and purkinje cells in the cerebelum. All of these cell types express aquaporin 1 or aquaporin 4. These results strengthen our hypothesis that there might be a functional correlation between taurine and water channels. This hypothesis will now be explored directly.

Body composition in dialysis patients treated with erythropoietin, measured by dual-energy x-ray absorptiometry. *D.I. Stenver, A. Gotfredsen, J. Hilsted, and B. Nielsen, Departments of Nephrology and Endocrinol-*

ogy, Copenhagen University Hospital, Hvidovre, Denmark. The aim of the present study was to examine the impact of erythropoietin (EPO) treatment on the body composition of dialysis patients. Body composition can be measured by dual-energy x-ray absorptiometry (DXA), a method which separates the principal components of the body into 3 main compartments: fat mass (FM), lean soft tissue mass (LSTM) comprising muscle, inner organs and the body water, and bone mineral content (BMC). Using this method we monitored body composition in 15 dialysis patients treated with recombinant human EPO. The patients were examined before and 6 months after the initiation of EPO treatment. The average hematocrit level at baseline was 26% and after 6 months 35%. A highly significant increase in FM, from 16,387 to 18,496 kg ($P = 0.0007$), was observed. The total body weight showed a mean increase of 0.955 kg (NS). The LSTM decreased by 1,185 kg (NS). Negligible fluctuations within the BMC compartment were observed. After having reached the target hematocrit level, several hypotensive episodes towards the end of a dialysis therapy were recorded in 8 patients, and in 3 of these patients a thrombosis of the arterio-venous anastomosis occurred. In conclusion, during a six-month period EPO treatment of terminal uremic patients is associated with a positive energy balance, reflected by a significant increase in FM. The adverse events are probably related to inappropriate fluid withdrawals. The DXA method is a useful tool for monitoring changes in BC of dialysis patients after an intervention, for example the initiation of EPO therapy.

Pregnancy in IgA nephropathy. *S. Rekola and H. Bucht, Department of Renal Medicine, Huddinge University Hospital, Karolinska Institute, Stockholm, Sweden.* Pregnancy is regarded as a risk factor in females with different types of glomerular diseases. In our patients with IgA nephropathy (IgAN), we make repeated determinations of GFR with clearance of Cr^{51}-EDTA. In nine patients we have GFR determinations before and after pregnancy. Mean age at delivery was 32 ± 5 years (range 24–43). All children were born alive. Two females had treatment for hypertension and six had proteinuria >1 g/24 hr prior to pregnancy. **Results:** GFR was 75 ± 23 ml/min/1.73 sqm BSA before and 75 ± 27 after pregnancy. Twenty-four hour urinary protein was 1.3 ± 1.8 g before and 1.1 ± 1.7 g after pregnancy. In two patients there was a significant increase in proteinuria during pregnancy, but they returned to their pre-pregnancy levels after delivery. An additional patient has developed hypertension two years after delivery. The patients were followed a further 3.5 years after delivery without any signs of a more aggressive disease. Among our female patients, not included in this study, 3 have developed ESRD. One became nephrotic during a pregnancy and started dialysis 2 years after delivery. Her previous history is unknown. Another patient became pregnant when GFR was 30 ml/min (Cr-EDTA). She also had heavy proteinuria and hypertension controlled with an ACE-inhibitor. When the ACE-inhibitor was withdrawn GFR decreased rapidly and she started dialysis one year after delivery. In the third patient the development of ESRD had no connection with pregnancies. **Conclusion:** Among our patients with IgAN normal GFR, we could not find any signs of decrease in GFR after pregnancy. Also patients with hypertension and a marked proteinuria tolerated a pregnancy without obvious side effects. In these patients pregnancy is not harmful. However, one patient had low GFR and a rapid deterioration of renal function during pregnancy. This may to some extent have depended on the withdrawal of an ACE-inhibitor, the use of which is contraindicated during pregnancy.

Angiography with non-ionic x-ray contrast media in severe chronic renal failure: Renal function and contrast retention. *K.J. Berg, J.Å. Jakobsen, K.P. Nordal, and J.Ø. Nossen, The National Hospital, University of Oslo, and Nycomed Imaging AS, Oslo, Norway.* The effects of contrast media on renal function and the cortical retention of contrast media after abdominal angiography were investigated. Sixteen non-diabetic patients with predialytic chronic renal failure received either the non-ionic dimeric contrast medium iodixanol or the monomeric contrast medium iohexol in a double-blind randomized study. All patients were well hydrated before, during and after angiography. Before angiography mean ^{99m}Tc-DTPA clearance was 14.0 ml/min/1.73 m^2 in the iodixanol group, and 9.3 ml/min/1.73 m^2 in the iohexol group, and mean serum creatinine 560 μmol/liter and 689 μmol/liter, respectively. No significant changes occurred in either group after angiography. Serum β_2-microglobulin and creatinine clearance were also unchanged. The urinary excretion of the renal enzymes alkaline phosphatase and N-acteyl-β-glucosaminidase and of total protein did not change significantly. No patients developed oliguria or required dialysis during the 7 day observation period. Increased attenuation in the renal cortex, measured by CT and probably reflecting intracellular retention of contrast medium, peaked at 24 hours, and was observed in both groups during the follow-up period. Thus, both iodixanol and iohexol were safe for use in angiography in non-diabetic patients with severe chronic failure when the patients were well hydrated.

Renal function parameters: Internal quality control and stability after freezing. *K.J. Berg, D.T. Kristoffersen, K.K. Lund, J. Narverud, and J.Ø. Nossen, Section for Nephrology, Medical Department B, The National Hospital, and Nycomed Imaging AS, Oslo, Norway.* This study was undertaken to (a) evaluate whether renal function parameters were stable during storage, (b) establish reference ranges for the parameters in fresh and stored samples, (c) compare overnight spot urine sampling versus 24 hour sampling in order to reduce the sampling burden for patients. A total of 150 healthy persons ranging from 20–70 years of age, with no known kidney disease, were to be included. The persons were stratified according to age and sex. The following parameters were analyzed in overnight spot urine and in 24 hour urine samples: alanine amino-peptidase (U-AAP), N-acetyl-β-glucosaminidase (U-NAG), alkaline phosphatase (U-ALP), creatinine, β-$_2$-microglobulin (U-β_2m) and U-albumin. Creatinine and β_2MG were also measured in serum, and creatinine clearance was calculated. The analyses were performed from the fresh samplings and then after 2 weeks, 2 months and 6 months storage at −20°C. All analyses, except for U-β_2m, were performed using a Cobas Mira spectrophotometer. U-β_2m was determined by the RIA method. Serum and urine values of creatinine and β_2m were unchanged after storage. U-albumin was reduced by 10% after 180 days. Urinary enzyme values were all reduced by storage, the U-ALP values being considerably decreased after 14 days. For the various parameters, overnight spot urine sampling gave appropriate correlation ($r > 0.6$) and information compared to 24 hour urine sampling.

Calcium channel blockade reduces renal vascular resistance during gradated obstruction of the pig ureter. *J.J. Hvistendahl, T.S. Pedersen, J.C. Djurhuus, and J. Frøkiær, Institute of Experimental Clinical Research, University of Aarhus, Aarhus, Denmark.* **Aim:** Unilateral ureteral obstruction (UUO) is associated with a marked reduction in ipsilateral renal function, likely caused by an active preglomerular vasoconstriction. Recently, calcium channel blockade was shown to preferentially dilate the preglomerular vessels in the hydronephrotic rat kidney. We examined the renal hemodynamic effects of a well-known calcium channel blocker (verapamil) in a pig model with unilateral gradated ureteral obstruction. **Methods:** Pigs were allocated to control or verapamil groups. Under general anesthesia ultrasonic flow probes were inserted around the renal arteries, and catheters placed in both renal veins and in the abdominal aorta for blood sampling and monitoring of aortic blood pressure (MAP). Catheters were also inserted in the ureters. Renal blood flow (RBF) was measured by transit time ultrasound and renal vascular resistance (RVR) as MAP/RBF. GFR was measured using a constant infusion clearance technique (renal extraction of ^{51}Cr-EDTA times the renal plasma flow). At onset of obstruction verapamil was given as a continuous infusion (7.5 μg/kg/min). Ureteral pressure was increased in steps of 10 mm Hg every 30 minutes until a maximum of 80 mm Hg was reached. **Results:** In controls ipsilateral RBF was reduced to 72 ± 8% during UUO, whereas contralateral RBF was maintained (105 ± 14%). In contrast, verapamil administration reduced both ipsilateral and contralateral RBF (67 ± 5% and 79 ± 4%, respectively). However, verapamil administration caused a significant reduction in MAP compared with control animals. Consequently, ipsilateral RVR was significantly reduced in the verapamil treated pigs compared with the untreated pigs (121 ± 9% vs. 153 ± 14%). Ipsilateral GFR was equally reduced in both groups. **Conclusion:** Following calcium channel blockade ipsilateral and contralateral RBF did not differ as opposed to the pronounced difference between the 2 sides in control animals. This suggests that an intact calcium channel is important for the increase in renal vascular resistance during UUO.

Risk factors in hemodialysis (HD) patients. Evaluation of commonly measured variables on death rate. *H. Løkkegaard and R. Klefter, Nefrological Department B, University Hospital of Herlev, Herlev, Denmark.* This study evaluates risk factors among commonly measured laboratory values and clinical findings in HD patients, followed by attempts to identify

optimal treatment strategies. Average plasma concentrations of albumin, protein, CO_2, urea, creatinine and average values of systolic and diastolic blood pressure together with information of sex, age, and renal diagnosis were related to survival rate in 210 sequences of hemodialysis treatments during a period of 94 months. The average treatment time was 12.6 (1–94) months. The materials were analyzed with stepwise regression using the Cox proportional hazard model (BMDP 2L), and actuarial life table analyses were performed to illustrate the magnitude of influence of the independent variables on patient survival (BMDP 1L). Patient survival was negatively correlated with age and positively correlated with average concentrations of albumin. Surprisingly, patient survival was negatively correlated to P-CO_2. Patient survival was significantly lower in diabetics.

Implementing a quality improvement project in a hemodialysis unit. *C. Warholm and J. Berglund, Renal Unit, Department of Medicine, Danderyd Hospital, Danderyd, Sweden.* **Aim:** To develop a system for continuous quality improvement in our hemodialysis unit. **Methods:** The impulse to develop a system in order to improve the quality of our dialysis care was an invitation from the University Hospital in Upsala to participate in a bilateral internal quality audit. After the audit we formed a "quality group," consisting of the upper management of the unit. We decided to concentrate on three areas and to aim for long-term results rather than rapid results. The three areas were revision of all P.M.s, organization and education. The staff was introduced to the project and most were eager to participate. We gave ourselves one year for this initial project and aimed at practical work rather than training the staff in various quality programs. **Results:** All P.M.s have been revised or are under revision in different working groups. Revised P.M.s have been renamed Information, Routine or Instruction, describing their respective purposes. Information on the revised documents is stored in a computer program, which gives rapid information on subject, author and date of revision. The staff has written job descriptions emanating from the tasks they actually perform. A new introduction and training scheme for new nurses has been written, designed to lead to a certificate of proficiency in hemodialysis treatment. **Conclusions:** Quality projects must be initiated by upper management. In order to arouse enthusiasm in the staff, projects must bear relation to everyday practice. If, for example, documents are revised by the people who actually treat the patients one is more likely to get useful working tools than if the documents are handed down by the management.

Calcium and sympathetic adrenal tone in female essential hypertension. *I. Os, G. Nordby, A. Westheim, and I. Eide, Department of Nephrology, Ullevål Hospital, Oslo, Norway.* **Aim:** To investigate the associations between total serum calcium, hypertension and plasma catecholamines in never-treated menopausal women (HT) and age-matched normotensive women (NT). **Methods:** All women were investigated between the 7th and 10th days of the menstrual cycle, and only one woman every day. Blood samples for adrenaline (A), noradrenaline (NA), dopamine (D), electrolytes and vasopressin (AVP) were drawn from indwelling venous catheters after 30 minutes recumbency. Blood pressure (BP) and heart rate (HR) were measured 3 times, and the average used for statistical analysis. A 24 hour urine specimen was collected for determination of electrolytes and creatinine excretion. **Results:** Mean total serum calcium did not differ between the NT and HT, but calcium correlated strongly to HR ($r = 0.82$, $P < 0.001$) in HT only. Furthermore, total serum calcium correlated to systolic BP ($r = 0.53$, $P < 0.05$) and pulse pressure ($r = 0.48$, $P < 0.05$) in HT only, while no such relationship was observed in NT. In multiple regression analysis with calcium, A, NA, BMI, only calcium and A turned out to be predictors of heart rate in HT. No association between HR or BP was observed with urinary excretion of calcium. **Conclusion:** The present findings indicate that the associations between calcium, heart rate and blood pressure in the hypertensive women may be the sympathoadrenal system.

Insulin resistance and sympathetic nervous system activity in premenopausal hypertensive women. *G. Nordby, A. Moan, S.E. Kjeldsen, I. Eide, and I. Os, Department of Internal Medicine, Ullevål Hospital, Oslo, Norway.* **Aim:** To compare insulin sensitivity and catecholamine responses to insulin in hypertensive (HT) and normotensive (NT) premenopausal women. **Methods:** HT (BP 149 ± 5/99 ± 2 mm Hg, $N = 14$) and NT (BP 128 ± 4/81 ± 2 mm Hg, $N = 12$) lean, matched for age, weight and body mass index (BMI) were studied with euglycemic glucose clamp technique and insulin sensitivity index [glucose disposal rate (GDR)/Insulin (I)] determined. Sympathetic nervous system activity was assessed by plasma adrenaline (A) and noradrenaline (NA) at baseline. **Results:** GDR/I correlated negatively with cholesterol in HT ($r = -0.57$, $P < 0.05$) and with BMI ($r = -0.42$, $P < 0.05$, $N = 26$). The response to euglycemic hyperinsulinemia in HT and NT differed with an increase both in A and NA. Fasting serum insulin and glucose did not differ between the two groups (16 ± 2 vs. 13 ± 1 mU/liter and 4.7 ± 0.1 vs. 4.9 ± 0.1 mmol/liter). GDR/I was also similar in HT (7.3 ± 0.8 a.u. and 7.6 ± 0.8 a.u.). **Conclusions:** Insulin sensitivity in lean, premenopausal women is not reduced compared to age- and weight-matched normotensive women, but they respond to hyperinsulinemia with increased sympathetic nervous system activity. An insulin-hyperadrenergic interaction may thus be of pathogenetic significance in lean hypertensive women.

Intra- and post-hemodialysis (HD) relationships between vena cava inferior diameter (VCID) and blood volume (BV). *J. Nisell, K. Katzarski, and J. Bergström, Departments of Internal Medicine Mora Lasarett, Mora and Renal Medicine Huddinge University Hospital, Stockholm, Sweden.* Post-HD VCID of between 8–11 mm/m^2 has been proposed as an index for attained "dry" weight. As the plasma refilling may continue post-HD, this study was undertaken to establish the relevant time for measurement of post-HD VCID. VCID was measured by ultrasonography intra-HD (240 min) and as well as post-HD (120 min); BV changes (%) were monitored "on line" simultaneously (In-Line Diagn., USA). At the end of HD, according to VCID, 8 of the patients (pts) were underhydrated, 1 normo-, and 1 overhydrated. Due to the post-HD refilling both BV and VCID increased ($P < 0.05$), as an equilibration state was attained after about 60–120 minutes. At that time, 5 of the pts were normo-, 2 over-, and 1 still underhydrated. We conclude that VCID measurements detect volume changes, but are useful only after BV refill is accomplished, that is 1–2 hours post-HD.

Dialysate sodium profile and intradialytic blood pressure. *P. Johansson, L. Karlsson, L. Lundberg, B.G. Stegmayr, and M. Svensson, Department of Internal Medicine, University Hospital, Umeå, Sweden.* The aim of the study was to evaluate the effect of two different sodium profiles upon the intradialytic blood pressure in patients treated with hemodialysis. **Materials and methods:** Seven patients (5 men, 2 women; mean age 70 years 54–82 years) treated with chronic bicarbonate hemodialysis were randomized to start with either a sodium at 148 mmol/liter and a linear decrease of dialysate sodium to 138 mmol/liter (H-L) after 4 hours and vice versa (L-H). Serum sodium and chloride as well as changes in blood pressure were studied. The dialysis machines used were AK100 and Hemophan hollow-fiber dialyzers (Gambro, Lund, Sweden). The conditions were identical except for the sodium profile for each patient for both dialysis runs. Mean values were calculated and paired statistics were used. **Results:** When using H-L, serum sodium changed from 138 to 142 mmol/liter ($P = 0.0006$), chloride from 94.9 to 98.7 ($P = 0.001$). Blood pressure was not changed significantly. When using L-H, serum sodium changed from 138 to 140 mmol/liter ($P = 0.004$), and chloride from 94.1 to 95.3 (NS). Blood pressure was not changed significantly. The number of hypotensive events between H-L and L-H was different. In conclusion, the sodium profile may cause considerable changes in the total body sodium and chloride content although the benefit on blood pressure and of the reduction of hypotensive episodes is less evident.

Innovative treatment of post-transplant lymphocele: Laparoscopic fenestration. *O. Øyen, A. Bakka, P. Pfeffer, B. Lien, A. Foss, Ø. Bentdal, P. Jørgensen, I.B. Brekke, and G. Sødal, Surgery Department B., Rikshospitalet, Oslo, Norway.* The incidence of lymphocele formation following renal transplantation has been reported as high as 18%. If the lymphocele results in impaired allograft function, leg edema, deep vein thrombosis or pelvic discomfort (due to size), the treatment of choice has traditionally been laparotomy and deroofing (fenestration), creating an internal drainage route for the lymph. However, since 1992 there has been an increasing number of case reports on successful laparoscopic treatment of this condition. We hereby present our material of 13 post-transplant lymphocele patients treated by laparoscopic deroofing from June 1993 to March 1995. In the same time period, 9 patients have been treated by conventional open surgery. These 22 patients give a Norwegian incidence of 6%

(22/360). Our laparoscopic method has resulted in 11 primarily successful cases, with a peritoneal window judged as satisfactory (improved/unaltered allograft function and fast recovery). However, in one patient the lymphocele recurred after one month, and reoperation with conventional open technique was performed. Preoperative injury occurred in two patients. In the first patient, a perforation of the renal pelvis had to be sutured via laparotomy. In the second patient, the bladder was "fenestrated" instead of the lymphocele (which was collapsed due to external drainage), and acknowledgment of this condition led to "open" reoperation after 3 days. In both patients the further course was uncomplicated without sequelae. In conclusion, laparoscopic deroofing of lymphocele offers several advantages, with minimal trauma to the patient and very fast recovery. However, the procedure is technically more demanding than should be expected, with a rather high risk of injury to closely related, vital structures. Even more harmful than our two major complications is transection of the ureter, which has been reported in two cases by others.

Phenotypic analysis of renal epithelial cells obtained from urine of renal transplant patients with different complications. *F. Gribanova and F. Baranova, Institute of Transplantology and Artificial Organs, Moscow, Russia.* Cytodiagnostic urinalysis was performed to estimate status of renal epithelial cells in renal post-transplant patients during acute rejection (AR, $N = 13$), acute tubular necrosis (ATN, $N = 12$), cyclosporine nephrotoxicity (CNT, $N = 9$) and stable renal function (SRF, $N = 13$). Forty-six patients during the first postoperative month were examined. Twenty ml of fresh urine were collected and centrifuged at 1500 rpm for 5 minutes. Immunocytochemical staining (APAAP) was conducted on cytocentrifuge preparations of urine sediment samples. The monoclonal antibodies used were anti-ICAM-1, VCAM (kindly provided by the Laboratory of Immunology, Edinburgh University), HLA-DR ("Medbiospectr", Moscow), anti-cytokeratin 18 (Boehringer Mannheim Biochemica). Statistical calculations were performed using Wilcoxon's U-test. AR demonstrated the highest activation of renal epithelial cells (REC) manifesting in increased % of ICAM+, VCAM+, HLA-DR+ cells (59.7 ± 5.8%; 46.8 ± 5.6%; 49.2 ± 5.3%, respectively; $P < 0.05$ vs. CNT, SRF). In ATN we saw the highest value of exfoliating REC and enhanced % of activated cells (ICAM+ cells- 25.5 ± 5.7%; VCAM+ cells- 12.4 ± 3.5%; HLA-DR+ cells- 34.5 ± 6.1%, $P < 0.05$ vs. CNT, SRF). Difference between AR and ATN groups in % of HLA-DR+ cells was not statistically significant ($P < 0.05$). CNT showed a significant increase in % of HLA-DR+ (20.8 ± 3.8%, $P < 0.05$ vs. SRF group), but not ICAM+, VCAM+ cells (14.2 ± 2.4%; 9.1 ± 2.5%, respectively). We conclude that immunologic conflict, ischemia and drug-induced toxicity lead to changes in the allograft renal epithelial cell's phenotype. The most significant changes occur in the acute rejection group.

Monitoring azathioprine therapy by measuring active metabolites in renal allograft recipients. *S. Bergan, H.E. Rugstad, Ø. Bentdal, A. Hartmann, B. Klemetsdal, J. Aarbakke, and O. Stokke, Rikshospitalet, Oslo and University of Tromsø, Tromsø, Norway.* A large variability of active metabolites, 6-thioguanine nucleotides (6-TGN) in red blood cells (RBCs), is observed when azathioprine (AZA) dosage in renal transplant recipients is based on body weight only. The aim of the present study is to evaluate the effect of individualizing AZA therapy by measurement of 6-TGN in RBCs. We also measure thiopurine methyltransferase (TPMT) activity and methylated mercaptopurine metabolites to reveal potential synergism with 6-TGN. In this prospective, open study, patients were randomized into either "high 6-TGN" or "low 6-TGN" groups, both also receiving cyclosporine and steroids. In the "high 6-TGN" group AZA is started at 5 mg/kg/day in order to obtain 6-TGN concentrations between 125 and 175 pmol/8 × 10^8 RBCs within the first postoperative days. Further dosing is maintained or tapered to keep 6-TGN concentrations within the same range. In the "low 6-TGN" group traditional dosing of AZA is used. In this group AZA dose is reduced below standard protocol if 6-TGN is above 75 pmol/8 × 10^8 RBCs; according to our experience this only occurs at such doses if renal function is significantly impaired. In both groups AZA is reduced if WBC drop below 4 × 10^9/liter. The patients are followed until 3 months after transplantation. During the last month AZA is tapered until 6-TGN is below 75 pmol/8 × 10^8 RBCs. Preliminary results indicate that biopsy verified rejection episodes may be less frequent in the "high 6-TGN" group, 7/17 (41%), than in the "low 6-TGN" group, 11/20 (55%). Nadir WBC was 3.8 × 10^9/liter vs. 4.4 × 10^9/liter, respectively. Dose reductions are frequent in both groups, and reactivated CMV may be more important than AZA in causing leukopenia. A formal interim analysis will be performed when 60 patients are evaluated in each group. In conclusion, the results so far indicate that AZA therapy may be optimized by measuring 6-thioguanine nucleotides in RBCs.

Five years follow-up of glomerular and tubular functions in heart transplant recipients. *A. Hartmann, A. Andreassen, H. Holdaas, S. Simonsen, P. Fauchald, and K.J. Berg, Medical Department B, National Hospital, University of Oslo, Norway.* **Aim:** Prospective evaluation of glomerular and tubular functions after heart transplantation (HTX) in recipients receiving triple immunosuppressive regimen including cyclosporine (CsA). Ten HTX patients (pts), nine males and one female averaging 49 years of age (range 24–60) were studied. **Results:** Data are presented as mean ± SEM. All pts completed the study; six were treated for hypertension, four received rejection therapy, none later than 6 months after HTX. The dose of CsA averaged 3.9 ± 0.3 mg/kg during the first year and 3.2 ± 0.3 mg/kg over the 4 last years.

Time after HTX	GFR, inulin *ml/min*	ERPF, PAH *ml/min*	Filtration fraction	Fractional reabsorption lithium
Basal, 3 months	66 ± 7	361 ± 42	19 ± 2%	0.58 ± 0.04
1 year	65 ± 6	297 ± 29	23 ± 1%	0.62 ± 0.03
5 years	66 ± 7	254 ± 21	26 ± 2%[a]	0.59 ± 0.04

[a] $P < 0.05$

Central hemodynamics measured by heart catheterization remained unchanged. Basal albumin excretion rate was 30 ± 13 μg/min, one year averaged 22 ± 9 μg/min increasing to 102 ± 32 μg/min at 5 years ($P < 0.05$); and for $\beta_2$microglobulin 931 ± 264 μg/24 hr, 904 ± 317 μg/24 hr and 1636 ± 551 μg/24 hr ($P = 0.16$), respectively. The excretion of tubular enzymes, NAG and ALP remained elevated but unchanged. **Conclusion:** CsA therapy over 5 years did not progressively impair glomerular or tubular functions in HTX patients. Whether the occurrence of microalbuminuria is related to CsA therapy, hypertension or other factors remains to be elucidated.

Adult polycystic kidney disease in a kidney transplant population. *H. Hadimeri, G. Nordén, and G. Nyberg, Transplant Unit, Sahlgrenska University Hospital, Göteborg, Sweden.* Disease manifestations in kidneys and other organs were recorded in a retrospective analysis of 116 patients with adult polycystic kidney disease (APKD) before and after kidney transplantation (Tx). **Patients:** Of the 874 first kidney Tx patients in Göteborg from 1985 to 1993, 116 (13.3%) had APKD (36% women). A dominant mode of inheritance was confirmed in 67%. Mean age (±SD) at end-stage renal failure was 51 ± 8 years, which was higher in women than in men ($P = 0.008$). **Transplantation:** Sixteen percent of patients had living donors and 26% were predialytic. Survival of patients and grafts after two years was 90 and 78%, not significantly different from 422 non-diabetic control patients aged ≥33 years in the same cohort. Follow-up time ranged 2–10 years, median 5. **Renal manifestations:** Nephrectomy was performed before Tx in 16% of the patients, 2/3 unilaterally, most often to create space for the transplant, and in 6% after Tx. **Extrarenal manifestations:** After Tx, 3 patients suffered perforation of the colon with peritonitis, one lethal, and a fourth patient had diverticulitis but no perforation. Two patients died of aortic aneurysms. Six percent of patients had suffered subarachnoidal hemorrages before Tx, but only one case was recognized among 13% with cerebrovascular events (CVI) during follow-up. Erythrocytosis was recorded with the first year in 25% of the patients and caused one CVI. One patient died of urothelial cancer. Most graft losses ($N = 41$) were caused by patients' death ($N = 16$) or rejection (21) but three followed renal artery thrombosis. No morbidity occurred in relation to liver cysts. **Conclusion:** APKD is a systemic disease, but renal and extra-renal manifestations had limited influence on the post-transplant course. Perforation of the colon and erythrocytosis were the most important specific risks related to Tx. The rather benign pre-transplant course may be a matter of selection.

Systemic vasculitis in a kidney transplant population. *P. Åkesson, G. Nordén, and G. Nyberg, Transplant Unit, Sahlgrenska University Hospital,*

Göteborg, Sweden. A thousand consecutive patients who received 1095 kidney transplants in Göteborg from 1985 to 1993 were evaluated with respect to their underlying renal disorder. The outcome for those with various forms of systemic vasculitis will be reported here. **Patients:** Of 30 patients who received 37 grafts, nine had microscopic polyarteritis (MPA) (12 grafts), seven Wegener's granulomatosis (WG), five Henoch-Schönlein's purpura (H-S) (6 grafts), three anti-GBM disease (5 grafts), three thrombotic thrombocytopenic purpura (TTP), two systemic sclerosis, and one rheumatoid arthritis (2 grafts). **Controls:** Two controls for each patient were picked from the consecutive file, matched for sex, age, living or cadaveric donor, and graft number. Study patients and controls were followed for 1–9, median 5 years. **Results:** Survival of patients (PS) and grafts (GS) did not differ between patients and controls at any time after transplantation. At the time of the last evaluation, GS was 23/37 (62%) for patients with vasculitis versus 66% for controls and PS was 27/37 (90%) versus 85% for controls. The median of serum creatinine was 120 versus 130 μmol/liter. The proportion of patients treated for rejection episodes during the first year after transplantation was also similar, 45 and 49%, respectively. Recurrent vasculitis occurred with six grafts; two WG (after 29 and 64 months), one MPA (13 months), two H-S (14 and 48 months), one TTP (34 months). Hematuria was often the initial sign. The patients received treatment directed against the disease, such as corticosteroids, cyclophosphamide and plasma exchange with fresh frozen plasma in the TTP case. Only the MPA graft was lost due to recurrence. **Conclusion:** Vasculitis may recur late after transplantation and threaten graft function. An awareness of this risk facilitates early institution of adequate treatment. Results of kidney transplantation to patients with systemic vasculitis may then equal those in other patients.